

Biomedical Imaging Image Registration & Uncertainty

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Department of Cybernetics

People

- ▶ 80 staff members, out of it
 - ▶ 40 teachers/researchers
 - ▶ 25 researchers
 - ▶ 15 technicians, administration
- ▶ 50 full time PhD students (8–10 PhDs/year)

Department of Cybernetics

Funding

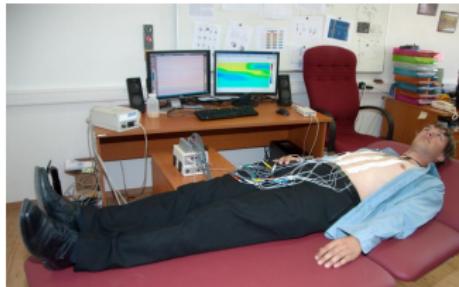
About 120–130 mil.CZK/year total, 60-70 mil.CZK salaries

- ▶ 30% institutional
 - ▶ 25% teaching
 - ▶ 75% research
- ▶ 70% external
 - ▶ CZ grants (50%)
 - ▶ EU, non-EU research grants (30%)
 - ▶ industrial collaboration (20%)

Biomedical data and signal processsing

Contact: doc. Lenka Lhotská, bio.felk.cvut.cz

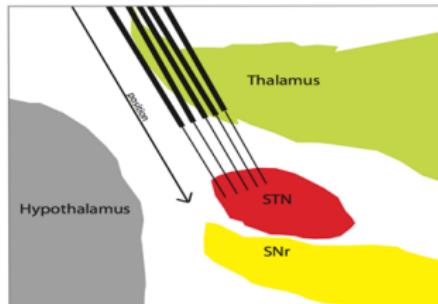
Expertise: biomedical signal processing (EEG,ECG), data mining & machine learning in medicine, decision support, telemedicine



Nature Inspired Technology

Contact: prof. Olga Štěpánková, nit.felk.cvut.cz

Expertise: Genetic algorithms, assistive technologies, tele-health & tele-care systems, data visualization & mining



Knowledge based and software systems

Contact: doc. Zdeněk Kouba, kbss.felk.cvut.cz

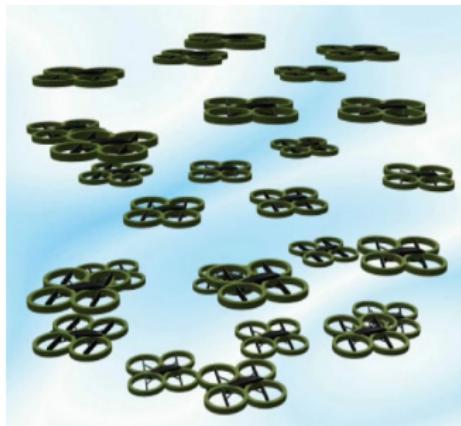
Expertise: Ontology based information systems, knowledge modelling, semantic web, OWL 2 reasoning, linked data, enterprise information systems

	α_i	$\mathcal{T}(\alpha_i)$
α_1	$A_1 \sqsubseteq \forall S \cdot A_2$	$A_1(?x) \wedge S(?x, ?y) \wedge \text{not}(A_2(?y))$
α_2	$A \sqsubseteq (\leq 1 S)$	$A(?x) \wedge S(?x, ?y_1) \wedge S(?x, ?y_2) \wedge \text{not} (?y_1 = ?y_2)$
α_3	$A \sqsubseteq (\leq n S)$	$\begin{aligned} &A(?x) \wedge \bigwedge_{1 \leq i \leq (n+1)} S(?x, ?y_i) \\ &\wedge \bigwedge_{i < j \leq (n+1)} \text{not} (?y_i = ?y_j) \end{aligned}$
α_4	$A \sqsubseteq (\geq n S)$	$\begin{aligned} &A(?x) \wedge \text{not} \left(\bigwedge_{1 \leq i \leq n} S(?x, ?y_i) \right. \\ &\left. \wedge \bigwedge_{i < j \leq n} \text{not} (?y_i = ?y_j) \right) \end{aligned}$

Intelligent and Mobile Robotics

Contact: Ing. Libor Přeučil, PhD., imr.felk.cvut.cz

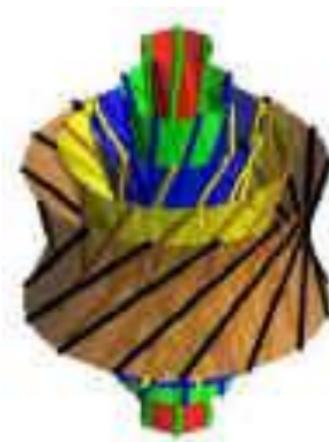
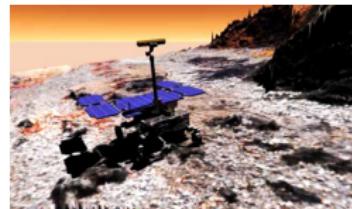
Expertise: intelligent mobile robotics, model building, self-navigation, mapping, collaboration, motion planning



Geometry of Vision and Robotics

Contact: Ing. Tomáš Pajdla, PhD. , cmp.felk.cvut.cz/~pajdla

Expertise: Geometry of cameras, manipulators & robots, 3D reconstruction from images, calibration, photogrammetry, algebra, optimization



Computer Vision (V. Hlaváč group)

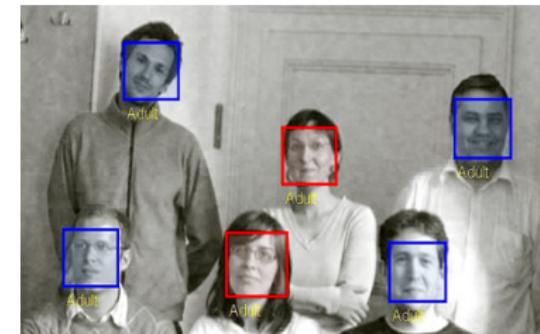
Contact: prof. Václav Hlaváč , cmp.felk.cvut.cz/~hlavac
Expertise: Computer vision, machine learning, robotics & manipulators, industrial applications



Pattern recognition (J. Matas group)

Contact: prof. Jiří Matas, cmp.felk.cvut.cz/~matas

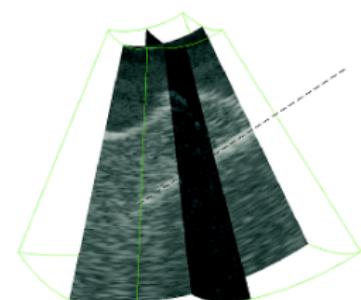
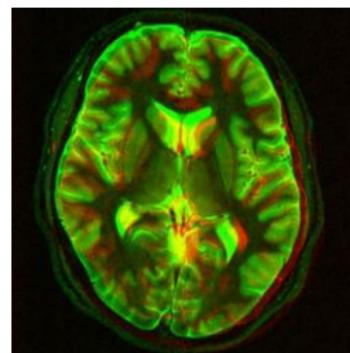
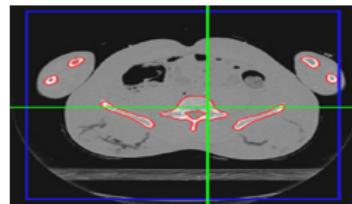
Expertise: Detection and recognition, image retrieval, tracking, categorization



Biomedical Imaging Algorithms

Contact: doc. Jan Kybic, cmp.felk.cvut.cz/~kybic

Expertise: Medical imaging, image analysis, image registration, segmentation & reconstruction



Jan Kybic

1994–1998 Ing., FEL ČVUT, technická kybernetika

1998–2001 Ph.D., EPFL, Lausanne, Švýcarsko, registrace, obrazů,
prof. Michael Unser

2001–2003 post-doc, INRIA, Sophia-Antipolis, Francie, MEG/EEG,
prof. Olivier Faugeras

2003–... FEL ČVUT

2010–2011 sabatický pobyt, EPFL, Lausanne, prof. Pascal Fua

2011 doc.

2011–2013 proděkan pro IT

2013–... vedoucí katedry kybernetiky

Biomedical Imaging Algorithms group

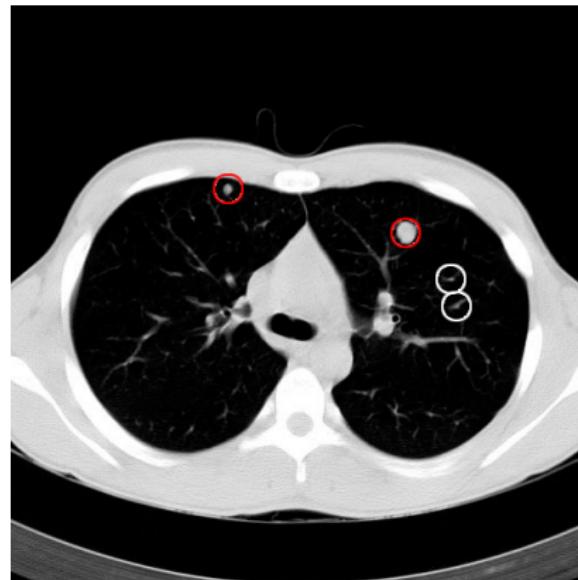
Postdoktorandi:

- ▶ Jan Švihlík
- ▶ Francisco Martínez
- ▶ Rodrigo Nava
- ▶ Thomas Dietenbeck (2013), François Varay (2012)

Doktorandi:

- ▶ J. Borovec (spolupráce U. Navarra)
- ▶ M-A. Pinheiro (spolupráce s EPFL, portugalský grant)
- ▶ M. Dolejší (spolupráce s nemocnicí v Motole, University of Iowa)
- ▶ J. Podlipská (univerzita v Oulu, konzultant)
- ▶ J. Krátký (spolupráce s FS ČVUT, přerušil)
- ▶ M. Uherčík (spolupráce s INSA, Lyon)
- ▶ J. Vandemeulebroucke (spolupráce s INSA, Lyon)
- ▶ J. D. García (nyní na U. Colombia)
- ▶ J. Petr (spolupráce s DkFZ Heidelberg)
- ▶ M. Barva (spolupráce s INSA, Lyon)

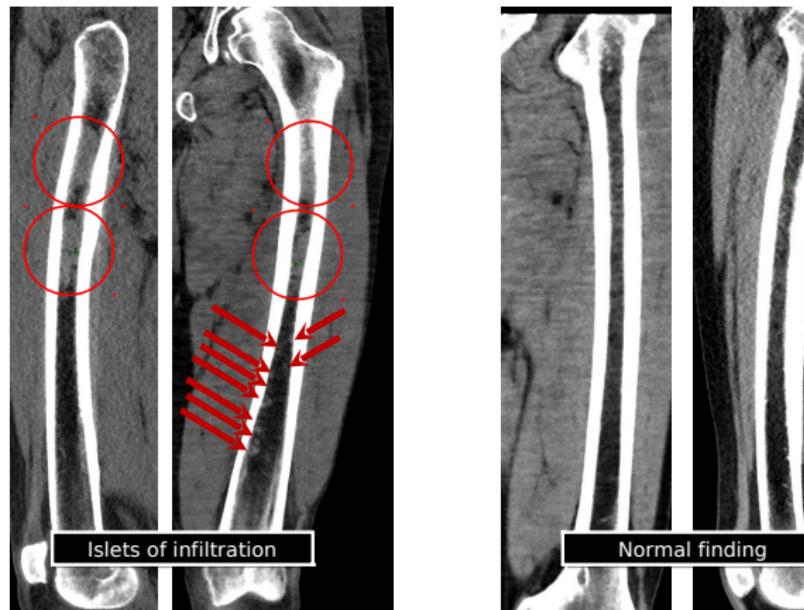
Detekce plicních nodulů z CT



Martin Dolejší, Iva Latnerová, nemocnice Motol

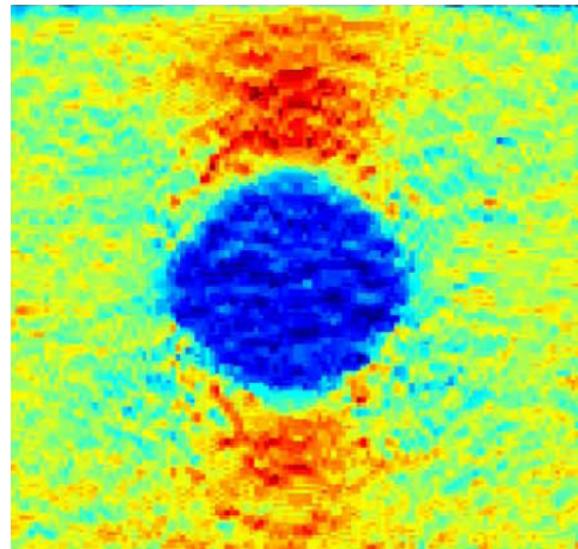
Segmentace dlouhých kostí

Detekce myelomu



VFN Praha, Francisco Martinez

Ultrazvuk

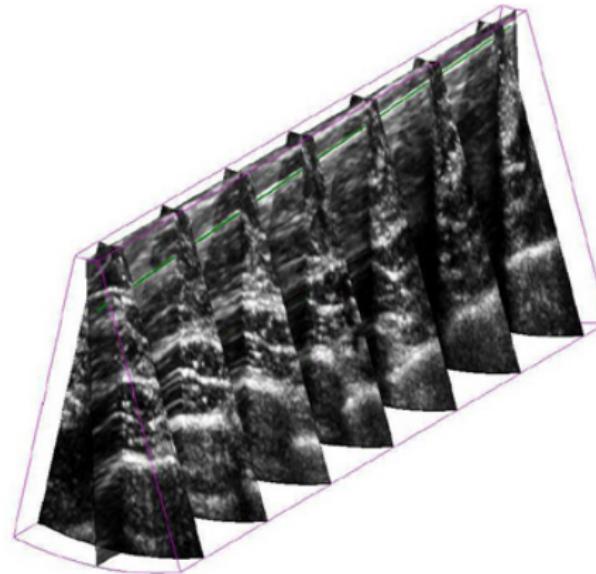


elastografie

Měření pohybu, elastografie, inverzní problém
disertace Praha–Lyon

Martin Barva, Marián Uherčík, s CREATIS, INSA Lyon, Francie

Ultrazvuk



3D ultrazvuk, detekce nástrojů

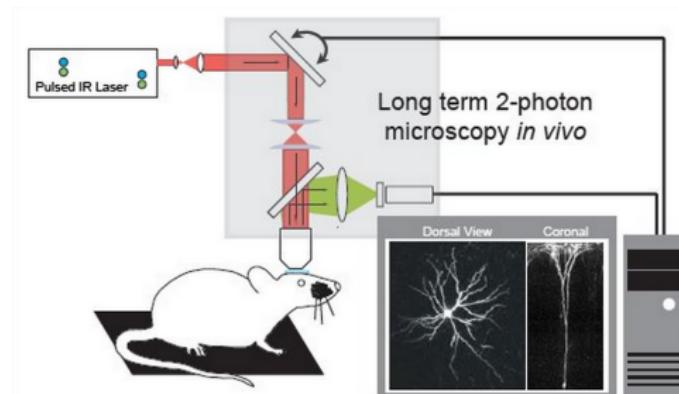
Měření pohybu, elastografie, inverzní problém
disertace Praha–Lyon

Martin Barva, Marián Uherčík, s CREATIS, INSA Lyon, Francie

3D mikroskopie nervových tkání

Segmentace, registrace, detekce změn

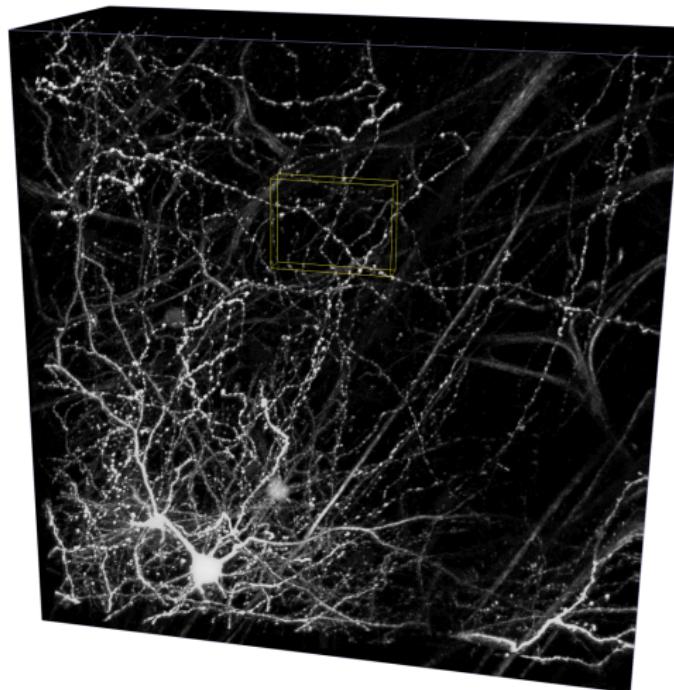
- ▶ Human Brain Project (EU flagship programme)
 - porozumět lidskému mozku.
- ▶ detektovat změny vlivem učení
- ▶ detektovat elementy, získat 'schéma zapojení' → simulace
- ▶ Miguel Amavel Pinheiro, s EPFL, Lausanne, Švýcarsko



Snímání.

3D mikroskopie nervových tkání

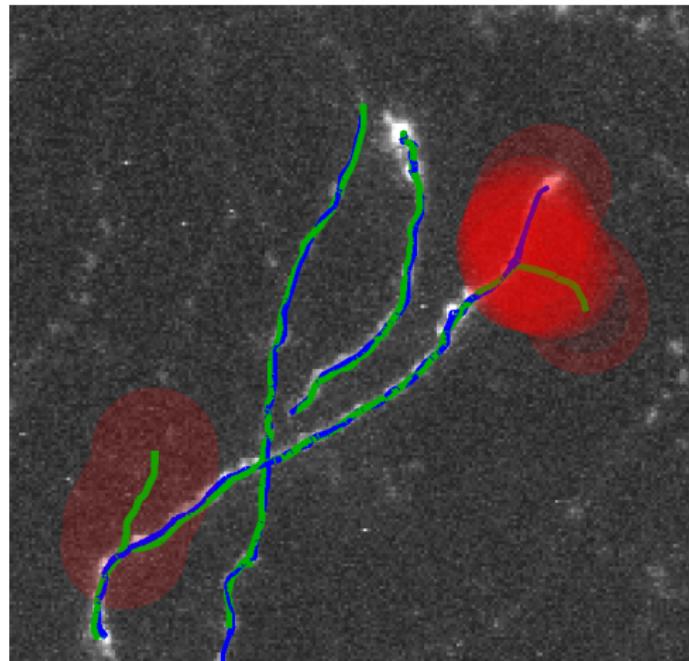
Segmentace, registrace, detekce změn



Dvoufotonová mikroskopie. (Two-photon microscopy)

3D mikroskopie nervových tkání

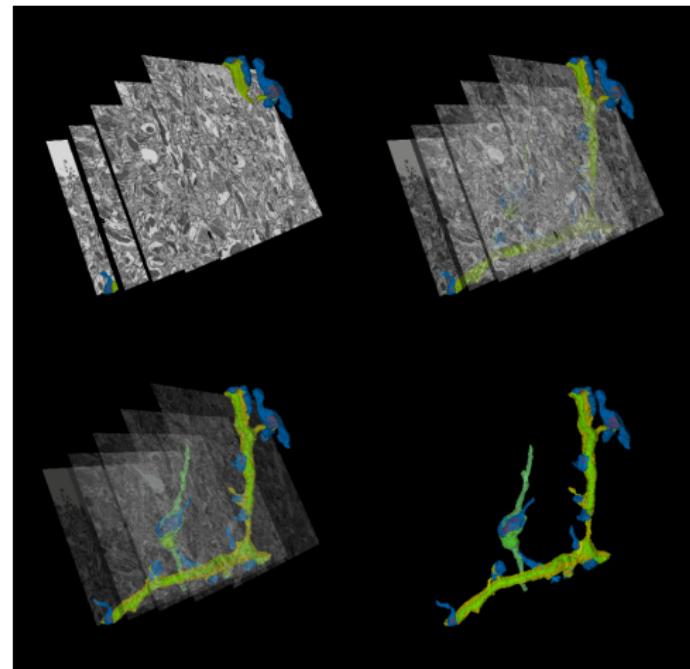
Segmentace, registrace, detekce změn



Detekce změn

3D mikroskopie nervových tkání

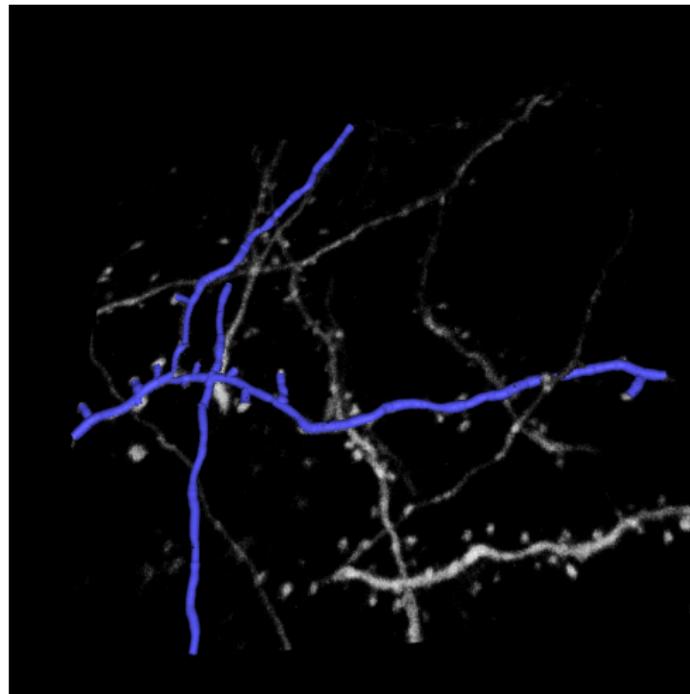
Segmentace, registrace, detekce změn



Elektronová mikroskopie + segmentace

3D mikroskopie nervových tkání

Segmentace, registrace, detekce změn

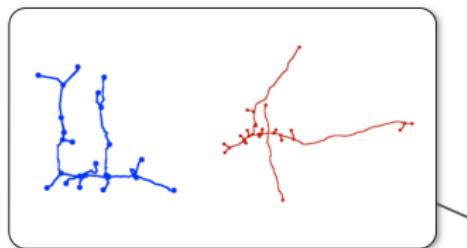


Světelná mikroskopie + segmentace

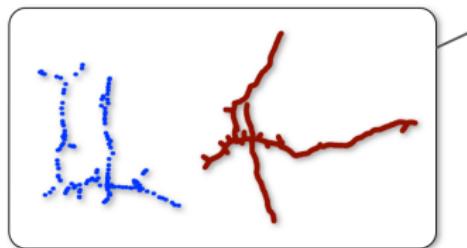
3D mikroskopie nervových tkání

Segmentace, registrace, detekce změn

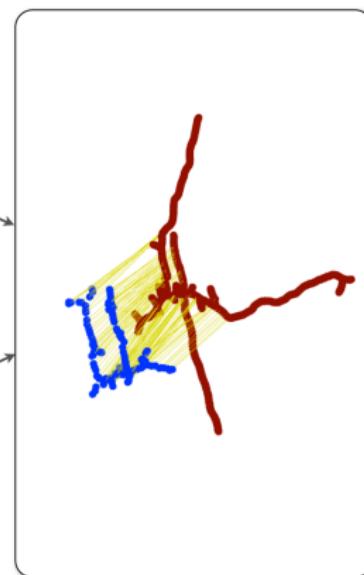
Graph representation



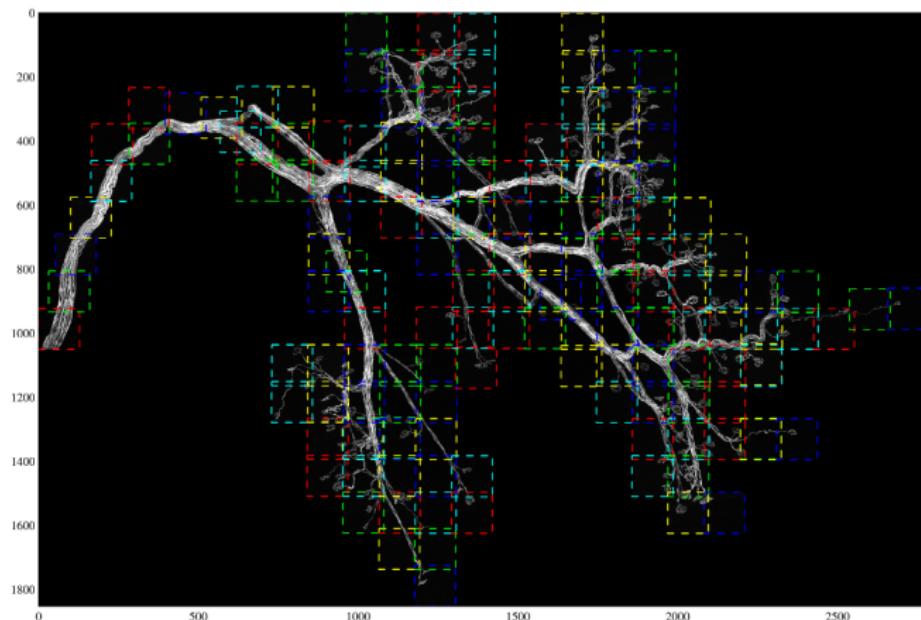
Point cloud representation



Registrace

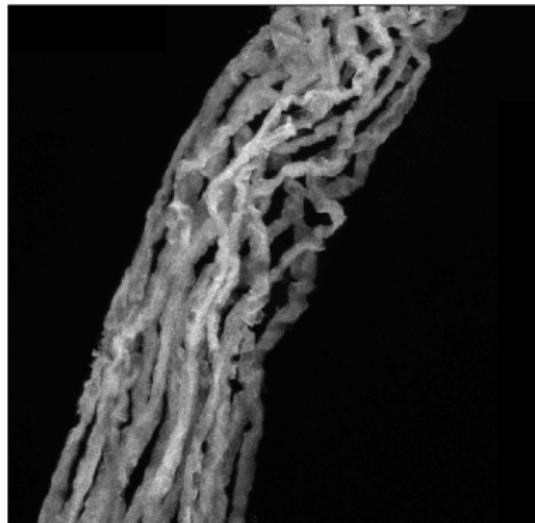


Sledování nervových vláken

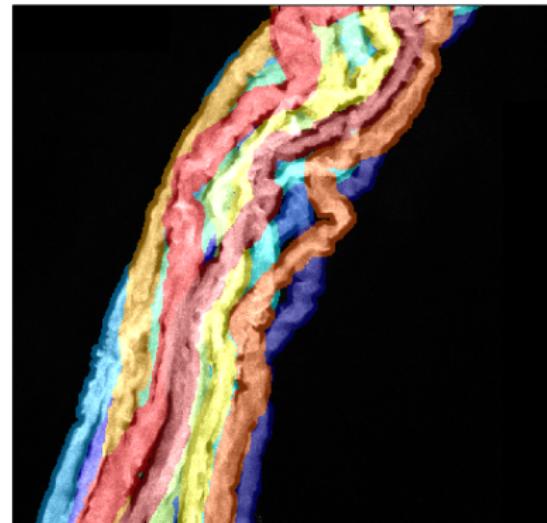


150 3D bloků $1024 \times 1025 \times 160$, 34GB

Sledování nervových vláken

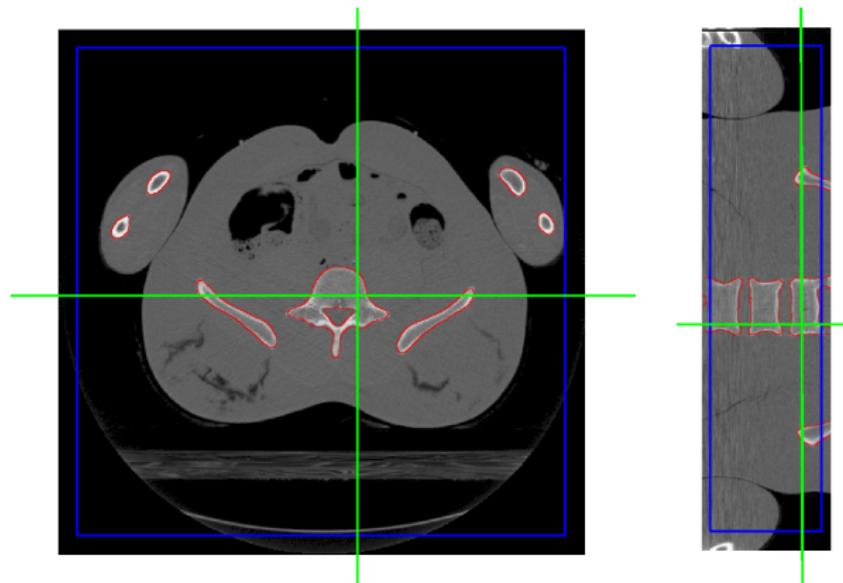


Initial image



Final segmentation

3D segmentace, rychlé diskrétní levelsety

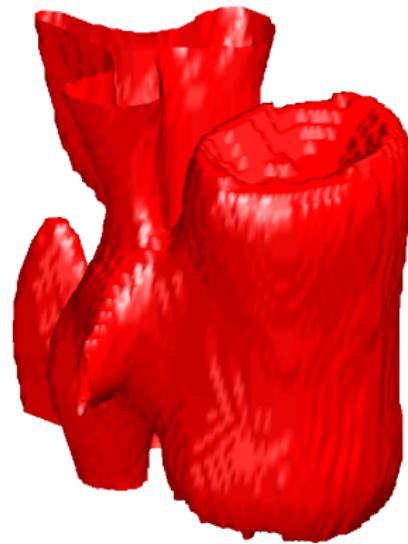


100× zrychlení

Možné téma: rozšíření pro registraci

Jakub Krátký

3D segmentace, rychlé diskrétní levelsety

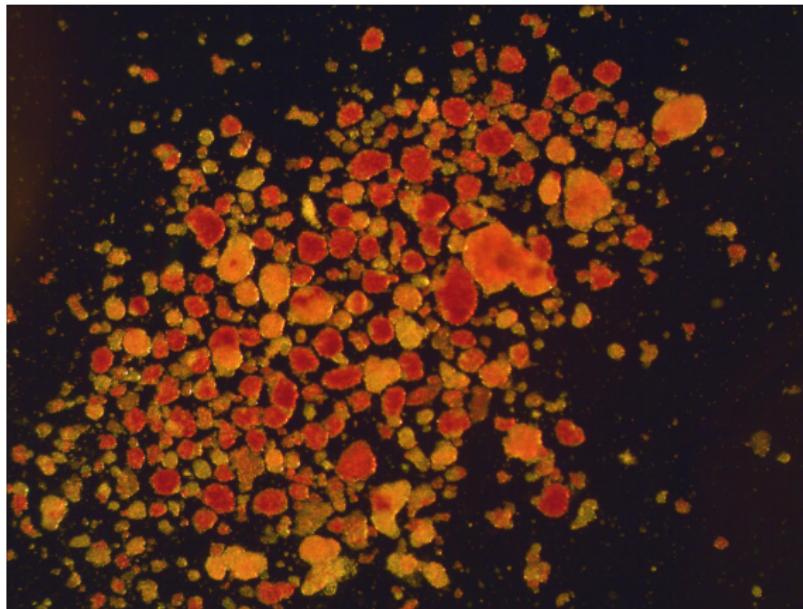


100× zrychlení

Možné téma: rozšíření pro registraci

Jakub Krátký

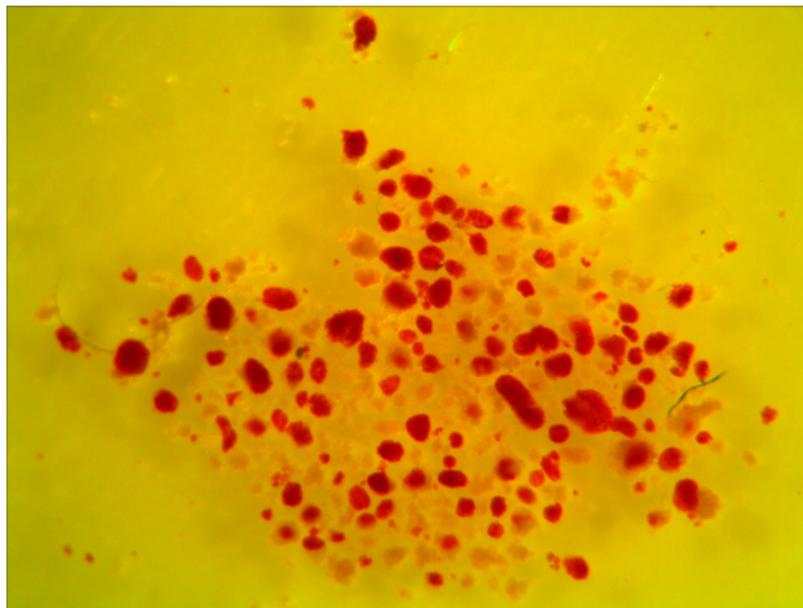
Detekce a počítání Langerhansových ostrůvků



Lengerhansovy ostrůvky, mikroskopie tmavého pole

Jan Švihlík

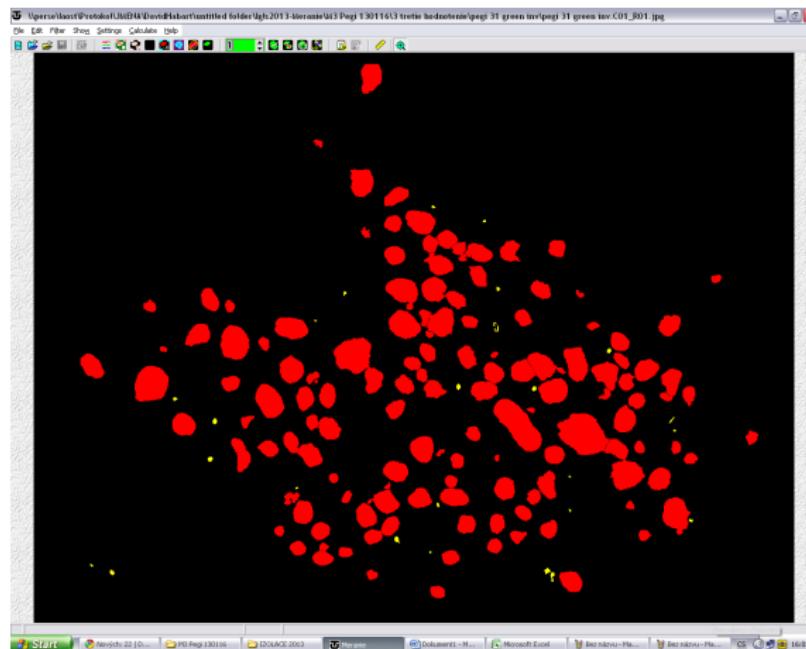
Detekce a počítání Langerhansových ostrůvků



Langerhansovy ostrůvky, mikroskopie jasného pole

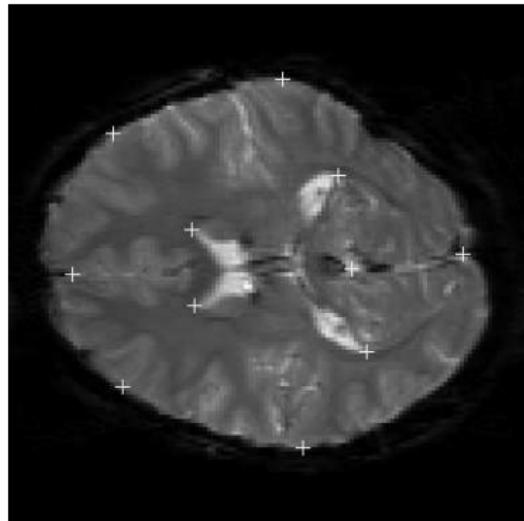
Jan Švihlík

Detekce a počítání Langerhansových ostrůvků

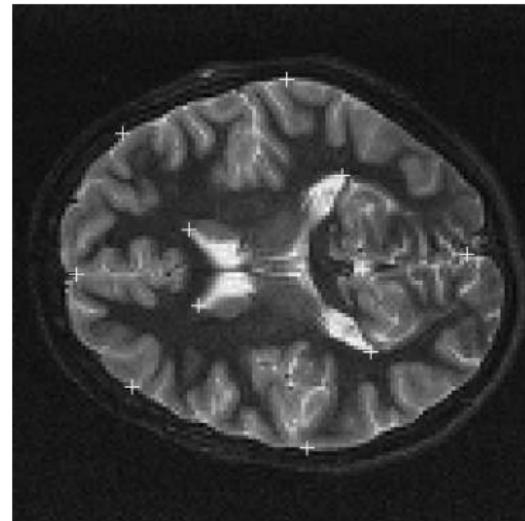


Segmentace

Registration example

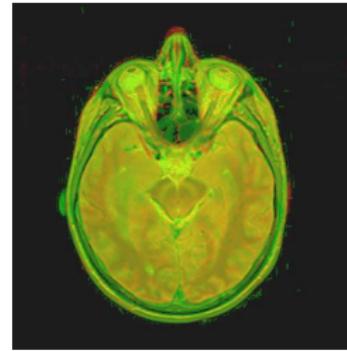
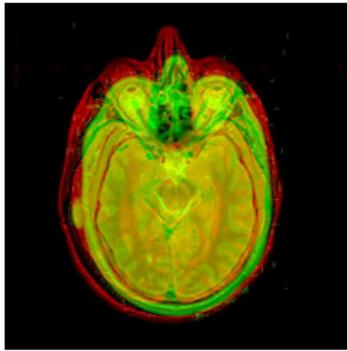
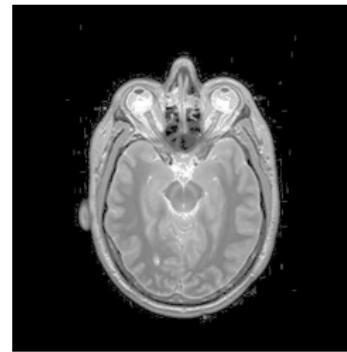
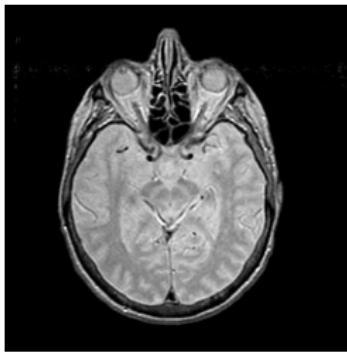


EPI MRI



anatomical MRI

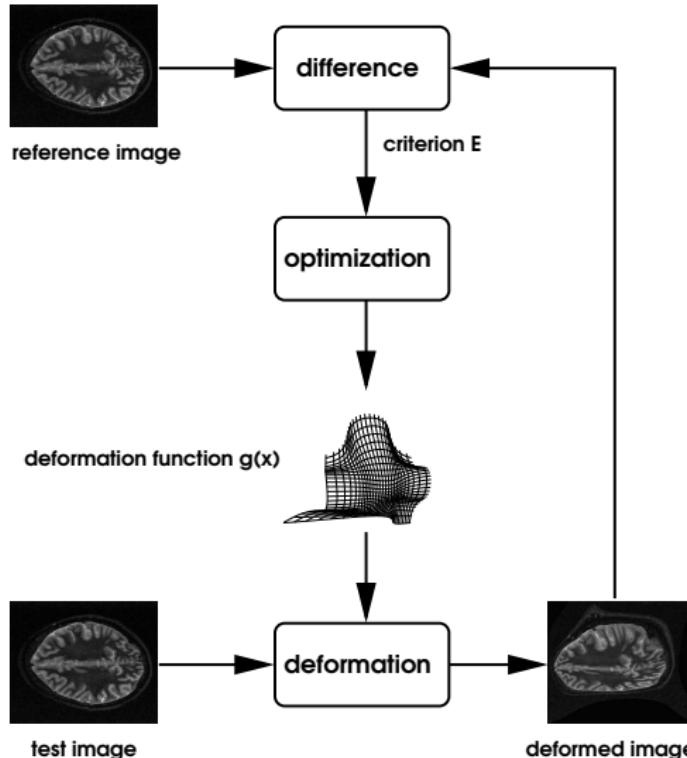
Image alignment



before

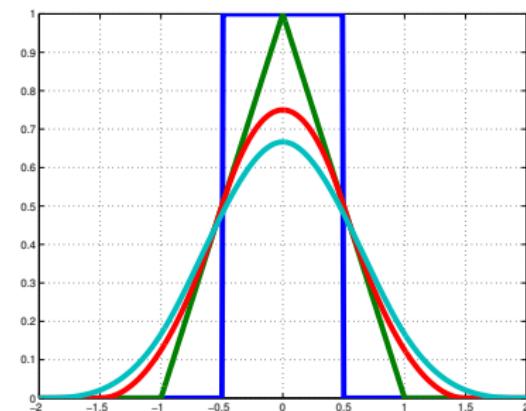
warped

Registration as minimization



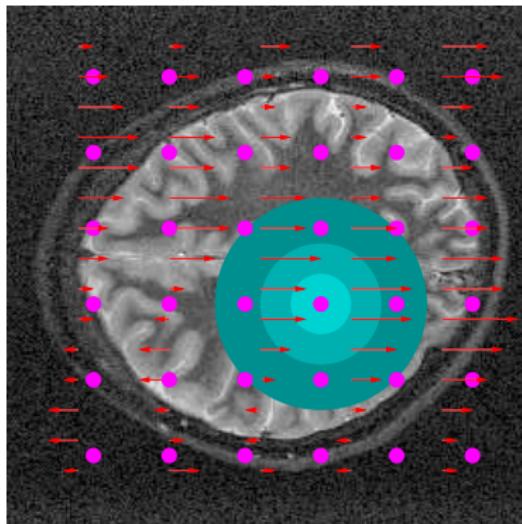
Uniform B-splines

Haar	β_0
linear	β_1
quadratic	β_2
cubic	β_3



- ▶ Generation: $\beta_{n+1} = \beta_n * \beta_0$
- ▶ Basis for splines: $s(x) = \sum_i c_i \beta(x - i)$

Spline based warping



- ▶ Approximation properties → precision
- ▶ Short support → speed
- ▶ Scalability
- ▶ Representability of linear transforms

$$\mathbf{g}(\mathbf{x}) = \mathbf{x} + \sum_{\mathbf{i} \in \mathbb{Z}^2} \mathbf{c}(\mathbf{i}) \beta(\mathbf{x}/\mathbf{h} + \mathbf{d} - \mathbf{i})$$

Applications

- ▶ EPI distortion

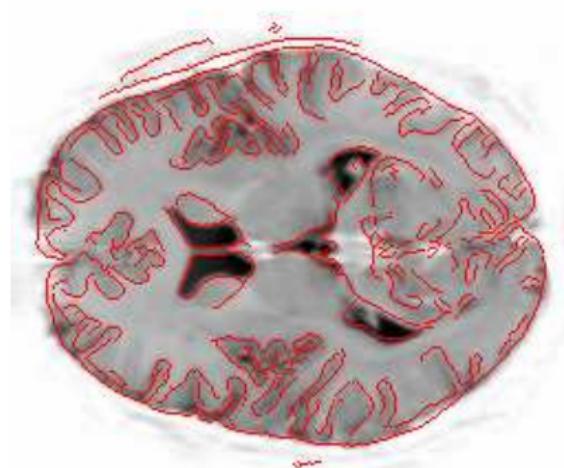


Before

(with Arto Nirko)

Applications

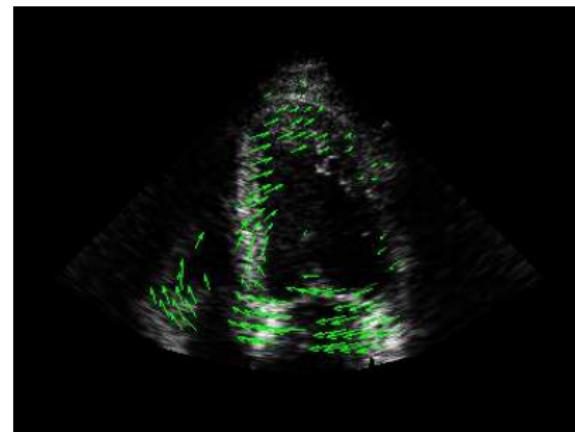
- ▶ EPI distortion



After

Applications

- ▶ EPI distortion
- ▶ Ultrasound



velocity

(with MarĂa J. Ledesma-Carbayo)

Colposcopy motion compensation

Template

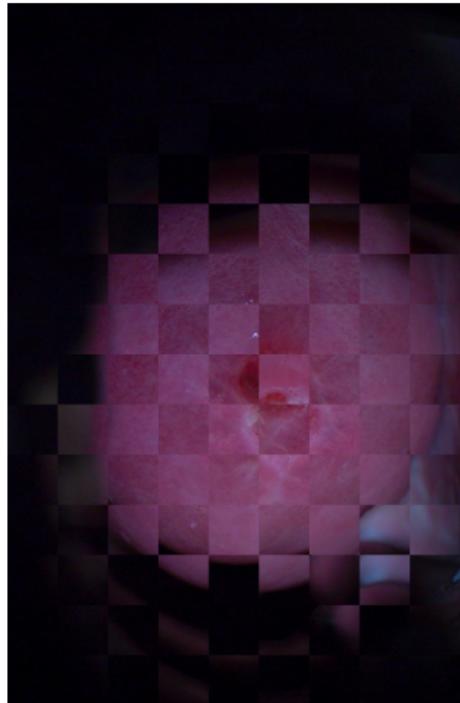


Moving

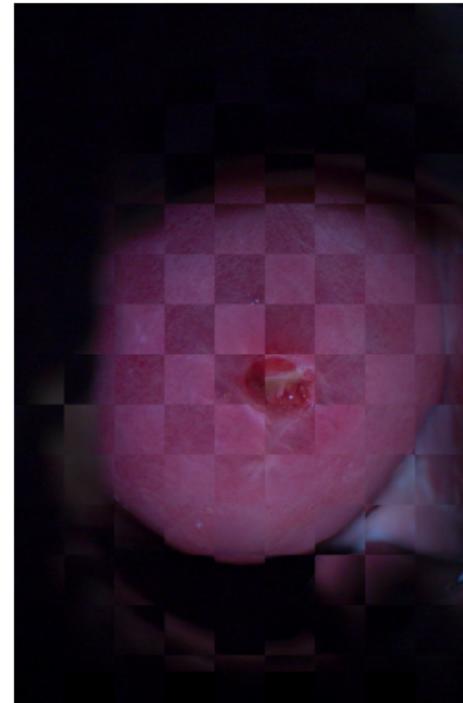


Colposcopy motion compensation

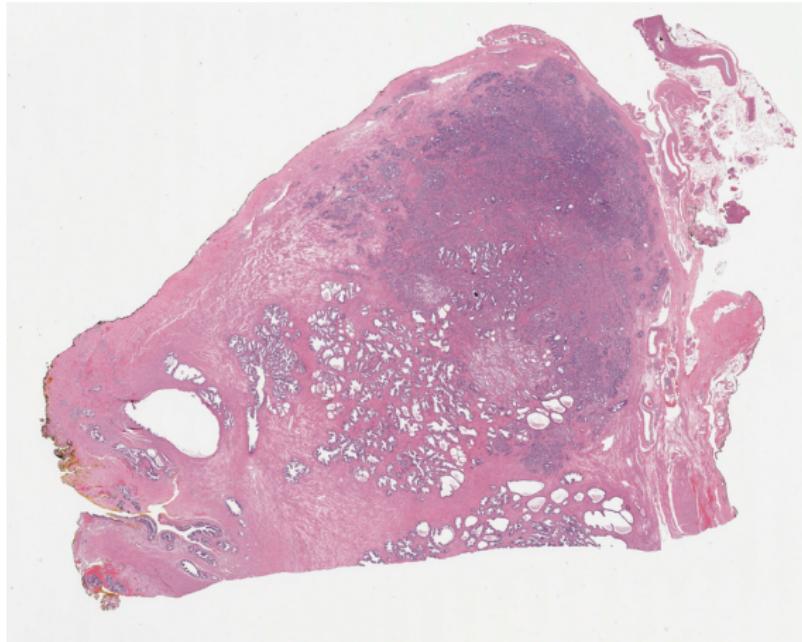
Unregistered Checkerboard



Registered Checkerboard

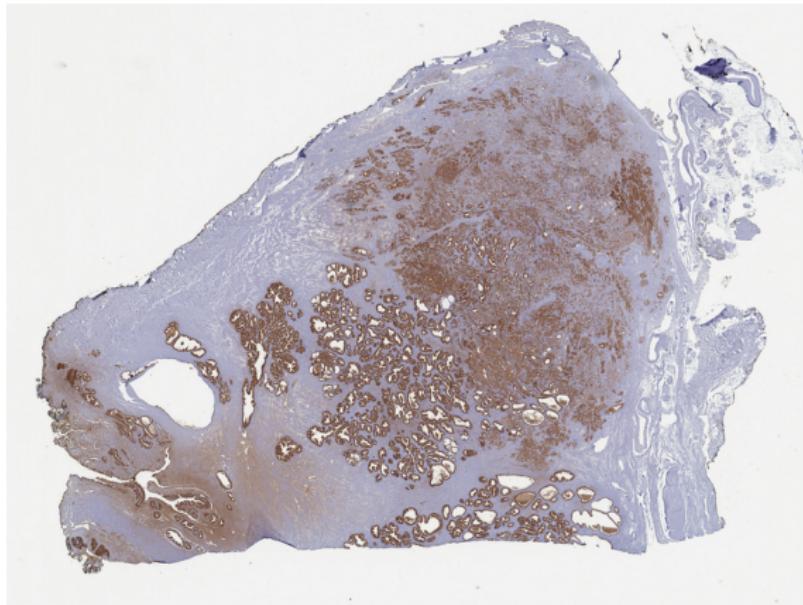


Registrace za pomocí segmentaci



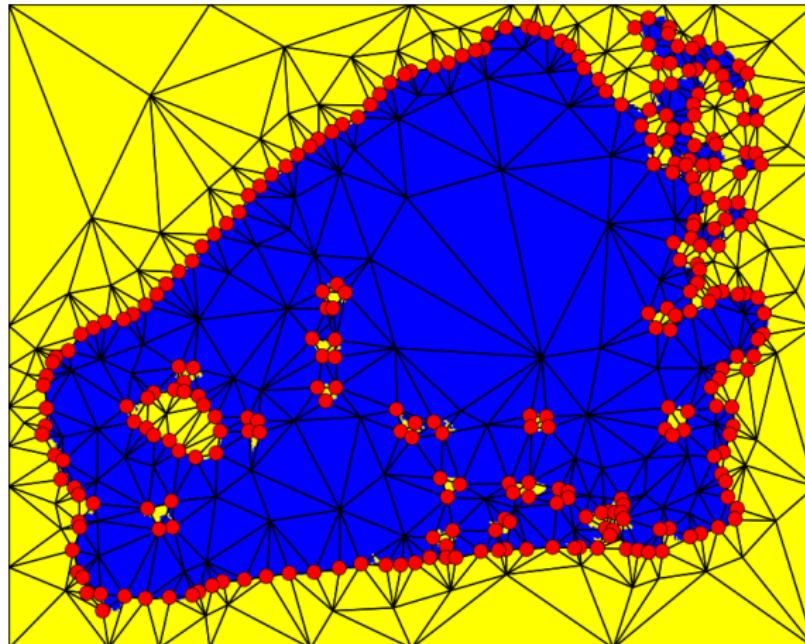
Prostata, barveno hematoxylinem a eosinem

Registrace za pomocí segmentaci



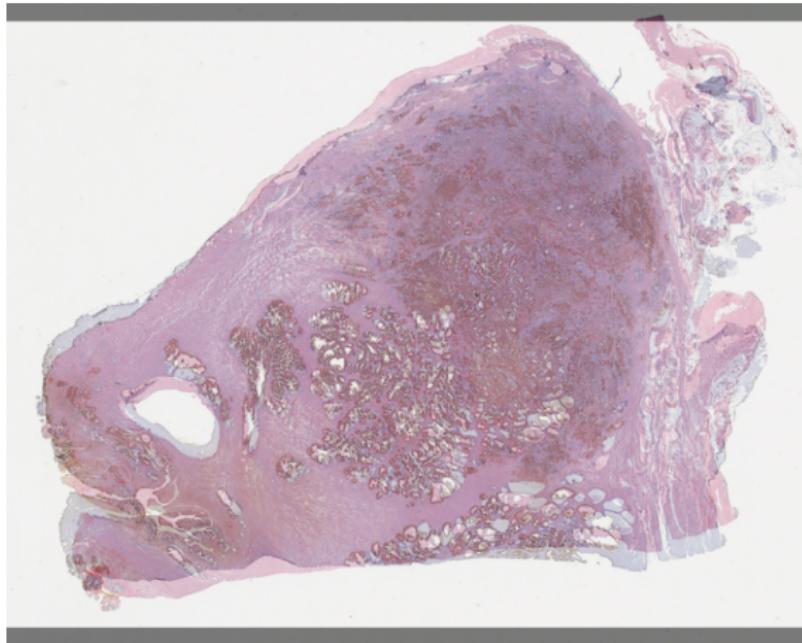
Prostata, barveno PSAP (anti prostate specific acid phosphatase)

Registrace za pomocí segmentaci



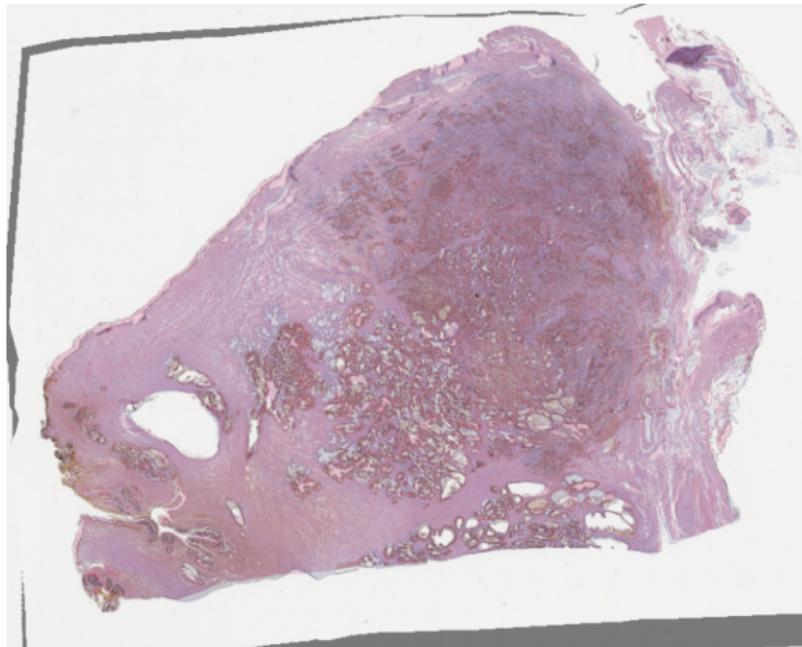
Segmentace, klíčové body, triangulace.

Registrace za pomocí segmentaci



Překrytí před registrací.

Registrace za pomocí segmentaci



Překrytí po registraci.

Podobná kvalita jako alternativy, ale mnohem rychlejší.

Image registration (problem definition)

- ▶ Image registration estimates a displacement field $\mathbf{x}' = T_\theta(\mathbf{x})$

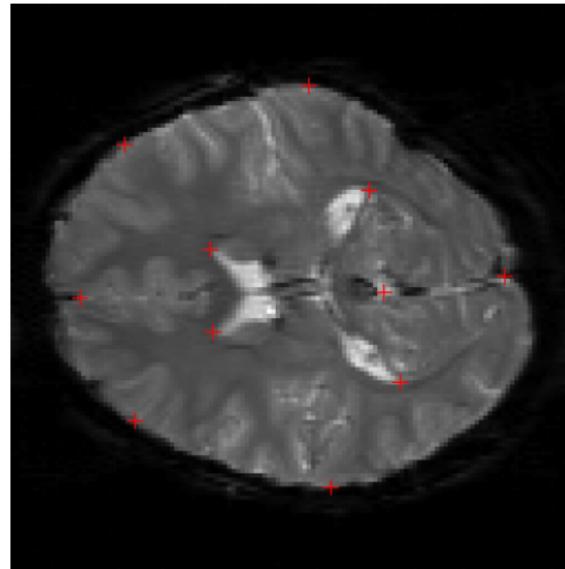
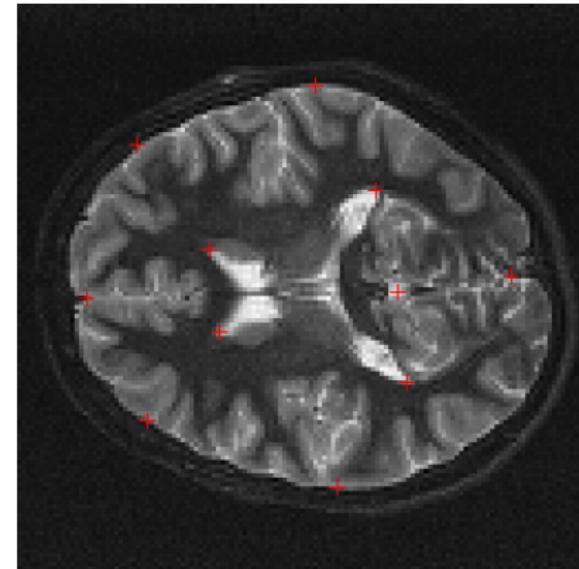
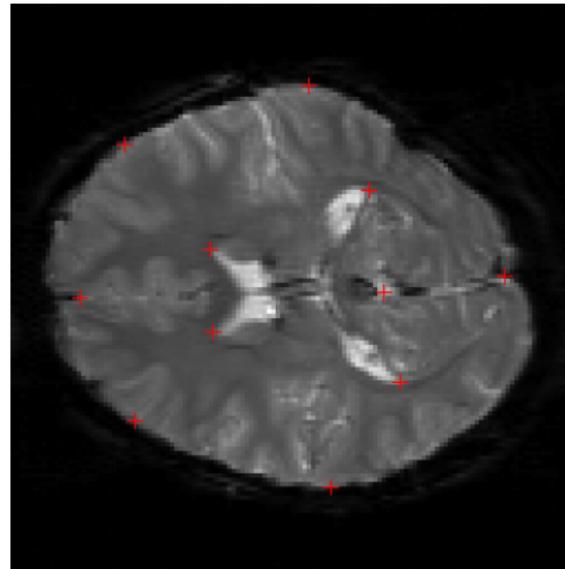
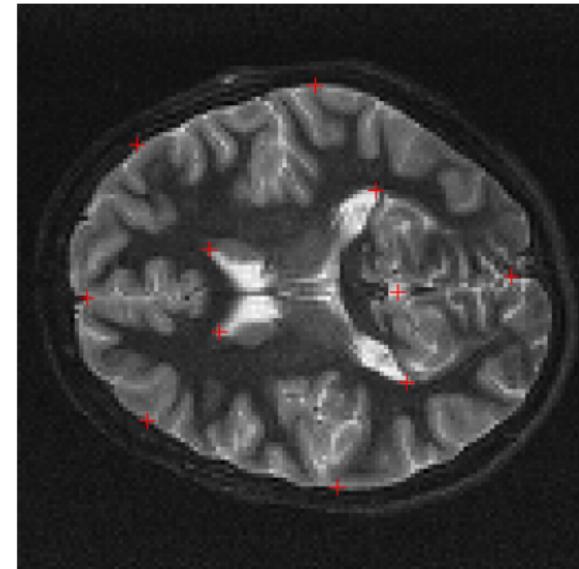
 $f(\mathbf{x})$  $g(\mathbf{x}')$

Image registration (problem definition)

- ▶ Image registration estimates a displacement field $\mathbf{x}' = T_\theta(\mathbf{x})$
- ▶ NEW: We shall also estimate its accuracy/reliability

 $f(\mathbf{x})$  $g(\mathbf{x}')$

Motivation for accuracy estimation (what is it good for)

- ▶ Can the registration results be trusted?
- ▶ Is the input data suitable?
- ▶ Weighting for further processing
 - ▶ Sequence registration
 - ▶ Group-wise registration
 - ▶ Post-processing, flow in-painting
 - ▶ *Elastography*: displacement → elastic parameters

Image registration + accuracy estimation

(a few simple equations)

$f, g \dots$ input images, $\mathbb{R}^n \rightarrow \mathbb{R}$, $n = 2 \dots 3$

$T_\theta \dots$ transformation $\mathbb{R}^n \rightarrow \mathbb{R}^n$, $\theta \in \mathbb{R}^d$

$\theta^* \dots$ true transformation parameters (unknown)

$$f(\mathbf{x}) \sim g(T_{\theta^*}(\mathbf{x}))$$

- ▶ **Image registration**

$$f, g \rightarrow \hat{\theta} \quad \hat{\theta} \approx \theta^*$$

Images f, g are one realization of a random process.

- ▶ **Accuracy estimation**

$$f, g \rightarrow \Psi[p(\hat{\theta} | f, g)]$$

Statistical properties of $\hat{\theta}$, resp. $\hat{\theta} - \theta^*$, such as $E[\|\hat{\theta} - \theta^*\|]^2$

Related work

(Image registration accuracy estimation)

- ▶ Ground truth data (gold standard)
- ▶ Mean of several methods (bronze standard)
- ▶ Heuristic uncertainty measures (data criterion based, high correlation coefficient)
- ▶ Penalize unlikely deformations (regularization criterion based)
- ▶ Indirect evaluation (e.g. via segmentation)
- ▶ Low-rank transformations (rigid motion) (Pennec 97)
- ▶ Noise and image model (Cramér-Rao bound)
(Robinson and Milanfar 2004, Yetik and Nehorai 2006)

Related work

(Image registration accuracy estimation)

- ▶ Ground truth data (gold standard)
- ▶ Mean of several methods (bronze standard)
- ▶ Heuristic uncertainty measures (data criterion based, high correlation coefficient)
- ▶ Penalize unlikely deformations (regularization criterion based)
- ▶ Indirect evaluation (e.g. via segmentation)
- ▶ Low-rank transformations (rigid motion) (Pennec 97)
- ▶ Noise and image model (Cramér-Rao bound)
(Robinson and Milanfar 2004, Yetik and Nehorai 2006)

What we want to do:

- ▶ No ground truth
- ▶ No noise and image model
- ▶ No transformation model
- ▶ ... only the two input images, f and g .

Block matching (to keep things simple)

- ▶ Translation only

$$T_\theta(\mathbf{x}) = \mathbf{x} + \theta, \quad \theta \in \mathbb{R}^2$$

- ▶ SSD similarity criterion

$$J = \sum_{\mathbf{x} \in \Omega} (f(\mathbf{x}) - g(T_\theta(\mathbf{x})))^2$$

block of pixels Ω — interval in \mathbb{Z}^2 .

- ▶ Optimal translation

$$\hat{\theta} = \arg \min_{\theta} J(\theta), \quad \theta \in I \subseteq \mathbb{R}^2$$

Accuracy estimation (for block matching)

What can we estimate:

- ▶ Mean and covariance

$$\mu_{\hat{\theta}} = \text{E} [\hat{\theta}]$$

$$\mathbf{C}_{\hat{\theta}} = \text{Var} [\hat{\theta}] = \text{E} \left[(\hat{\theta} - \mu_{\hat{\theta}})^T (\hat{\theta} - \mu_{\hat{\theta}}) \right]$$

- ▶ Mean geometrical error (warping coefficient)

$$\varepsilon^2 = \text{E} \left[\underset{\mathbf{x} \in \Omega}{\text{mean}} \| T_{\hat{\theta}}(\mathbf{x}) - T_{\theta^*}(\mathbf{x}) \|^2 \right]$$

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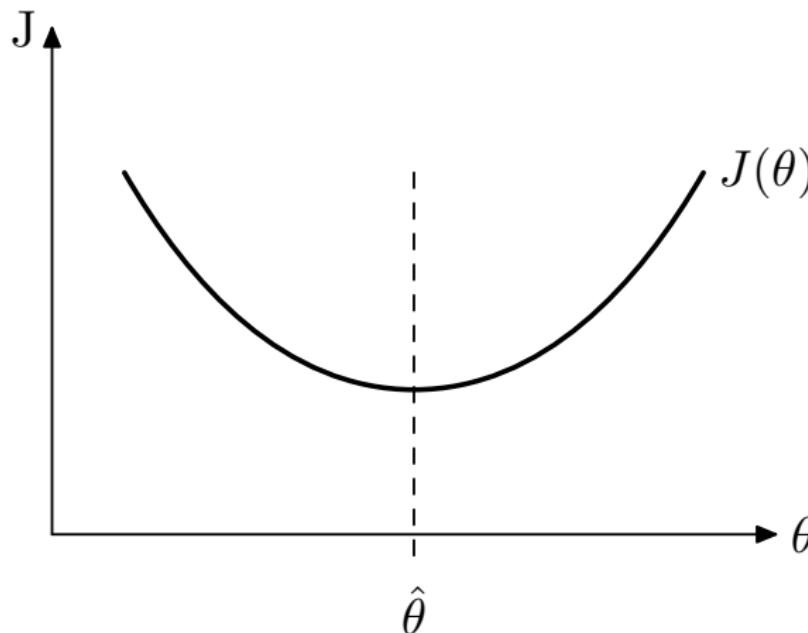
$$\varepsilon^2 = \text{E} \left[\underset{\mathbf{x} \in \Omega}{\text{mean}} \| T_{\hat{\theta}}(\mathbf{x}) - T_{\theta^*}(\mathbf{x}) \|^2 \right] = \text{tr} \mathbf{C}_{\hat{\theta}}$$

since $T_{\theta}(\mathbf{x}) = \mathbf{x} + \theta$

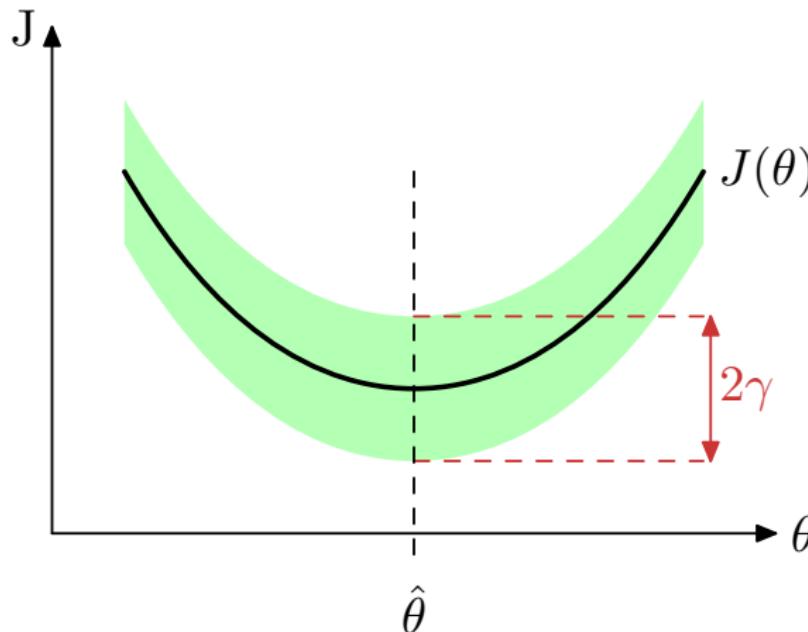
Fast registration accuracy estimation (FRAE) (Method I)

- + Fast, minimal overhead.
- Approximate, a lot of assumptions...

Fast registration accuracy estimation (FRAE) (Method I)



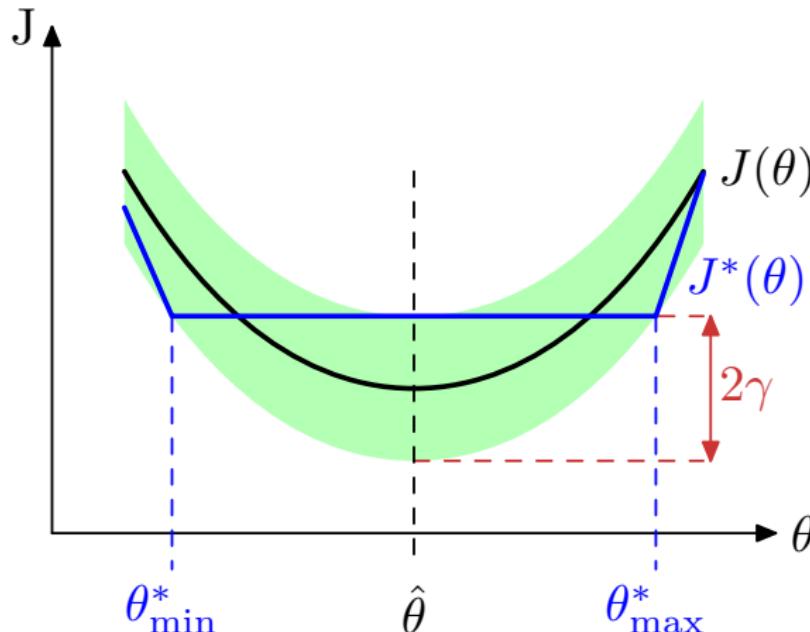
Fast registration accuracy estimation (FRAE) (Method I)



1. Confidence interval on the criterion J

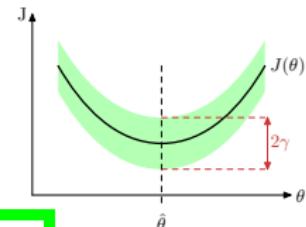
$$\hat{\theta} = \arg \min_{\theta} J(\theta)$$

Fast registration accuracy estimation (FRAE) (Method I)



1. Confidence interval on the criterion J
$$\hat{\theta} = \arg \min_{\theta} J(\theta)$$
2. Uncertainty of $\hat{\theta}$

Confidence interval on the criterion (FRAE, first step)



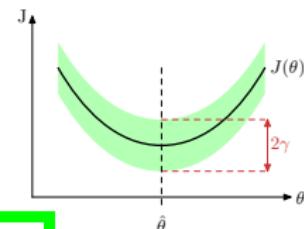
$$P[J^* - \gamma \leq J \leq J^* + \gamma] = 1 - \alpha$$

$$\alpha = 0.05$$

J ... measured criterion

J^* ... true criterion

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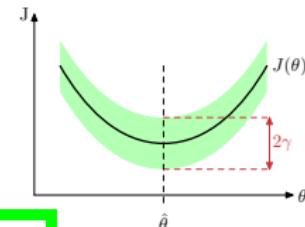
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J ... measured criterion J^* ... true criterion

- ▶ Assume the normality of $J - J^*$:

$$\gamma = \Phi^{-1}(1 - \alpha/2) \sigma_J \approx 1.96 \sigma_J$$

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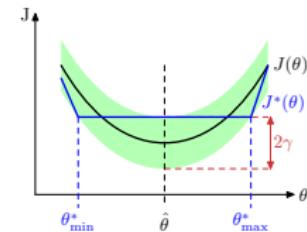
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- ▶ For $J = \sum_{\mathbf{x} \in \Omega} e(\mathbf{x})$ with $e(\mathbf{x})$ approximately i.i.d.:

$$\sigma_J^2 = N \text{Var}[e] \approx \sum_{\mathbf{x} \in \Omega} (e(\mathbf{x}) - \frac{1}{N} \sum_{\mathbf{x} \in \Omega} e(\mathbf{x}))^2$$

Uncertainty of $\hat{\theta}$

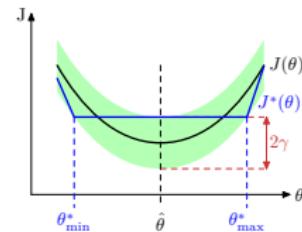
(FRAE, second step)



$$\min J^* = J^*(\theta^*) \Rightarrow J^*(\theta^*) \leq J^*(\hat{\theta})$$

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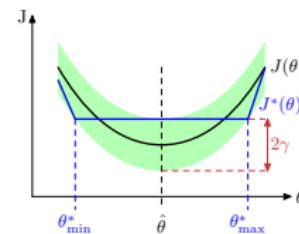


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confidence interval \Rightarrow $J(\theta^*) - \gamma \leq J^*(\theta^*)$ with probability $1 - \alpha$
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 $J(\hat{\theta}) + \gamma \geq J^*(\hat{\theta})$ with probability $1 - \alpha$

Combining these inequalities yields:

$$J(\theta^*) \leq J(\hat{\theta}) + 2\gamma$$

with probability $(1 - \alpha)^2$

Covariance of $\hat{\theta}$

(FRAE, continuation of the second step)

$$J(\theta^*) \leq J(\hat{\theta}) + 2\gamma \quad \text{with probability } (1 - \alpha)^2$$

- ▶ Quadratic approximation of $J(\theta)$:

$$J(\theta) = J(\hat{\theta}) + \frac{1}{2}(\theta - \hat{\theta})^T \mathbf{H}(\theta - \hat{\theta})$$

is available *for free* from the BFGS optimizer

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- ▶ Equivalent covariance matrix (as if $\hat{\theta}$ was normal)

$$\mathbf{C}_{\hat{\theta}}^{\text{FRAE}} = \frac{4\gamma}{F^{-1}((1-\alpha)^2, d)} \mathbf{H}^{-1} \propto \sigma_J \mathbf{H}^{-1}$$

Bootstrap registration accuracy estimation (Method II)

- + General, extensible to most pixel-based registration techniques
- Slow, high computational complexity

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Assumptions to make (FRAE needs them too):

- ▶ Independent pixels (features)
- ▶ Ergodicity
- ▶ Smoothness of the criterion
- ▶ Relevance of the criterion

Bootstrap — Problem definition (the miracle)

Given samples $\mathbf{X} = \{x_1, \dots, x_N\} \sim \text{pdf } \mathcal{X}$.

- ▶ Estimator $\hat{\vartheta}(\mathbf{X})$ of a statistics $\vartheta(\mathcal{X})$
(statistics = function of \mathcal{X} , e.g. mean, variance, ...)
- ▶ Estimate the accuracy of $\hat{\vartheta}$ (variance, confidence interval)
- ▶ ... using only data \mathbf{X}

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Alternatives

- ▶ Cross-validation
- ▶ Leave-one-out, jackknife estimate

Bootstrap resampling (how it works)

- ▶ Given samples $X = \{1, 3, 4, 2, 3, 5, 7, 1, 3, 3\}$.
- ▶ Randomly resample from X with replacement
→ **M bootstrap samples** (multisets, no ordering)

$$B_X^{(1)} = \{3, 3, 3, 3, 5, 3, 3, 3, 7, 3\}$$

$$B_X^{(2)} = \{7, 3, 2, 1, 3, 3, 4, 7, 3, 7\}$$

$$B_X^{(3)} = \{1, 3, 3, 7, 2, 1, 3, 1, 7, 3\}$$

$$B_X^{(4)} = \{3, 3, 1, 3, 3, 3, 2, 2, 4, 3\}$$

...

$B_X^{(b)}$ conditionally independent wrt X ; $B_X^{(b)} \sim X \sim \mathcal{X}$

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...

$B_X^{(b)}$ conditionally independent wrt X ; $B_X^{(b)} \sim X \sim \mathcal{X}$

- ▶ Evaluate $\hat{\vartheta}^{(b)} = \hat{\vartheta}(B_X^{(b)})$
- ▶ The pdf of $\hat{\vartheta}(\mathcal{X})$ is approximated by $\hat{\vartheta}^{(1)}, \dots, \hat{\vartheta}^{(M)}$.

Bootstrap for accuracy estimation (how to apply it)

$$J(\theta; \Omega) = \sum_{\mathbf{x} \in \Omega} e(\mathbf{x}; \theta)$$

allow for multiset Ω

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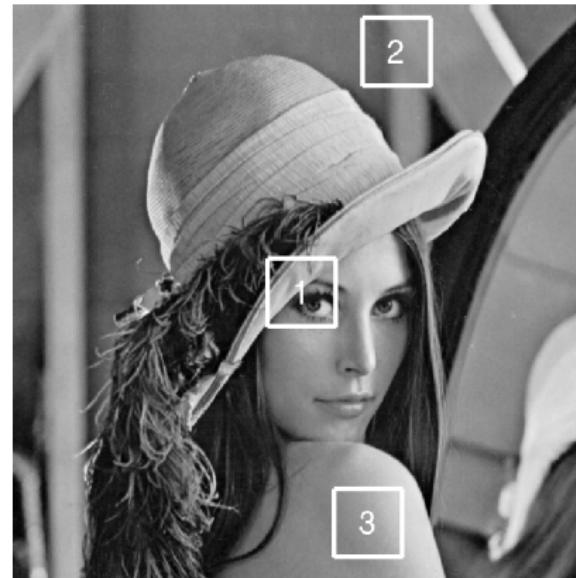
- ▶ Make M bootstrap data (multi)sets $\Omega^{(b)}$ by resampling Ω .
- ▶ Perform registration for each $\Omega^{(b)}$
- ▶ Evaluate the desired statistics of $\hat{\theta}$:

$$\mu_{\hat{\theta}}^{\text{boot}} = \frac{1}{M} \sum_{b=1}^M \hat{\theta}^{(b)}$$

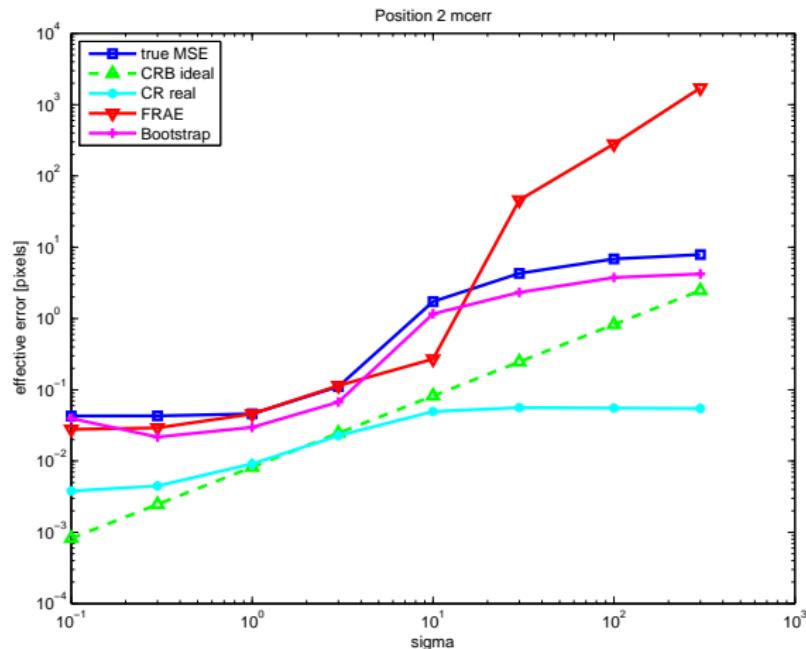
$$\mathbf{C}_{\hat{\theta}}^{\text{boot}} = \frac{1}{M} \sum_{b=1}^M (\hat{\theta}^{(b)} - \mu_{\hat{\theta}}^{\text{boot}})^T (\hat{\theta}^{(b)} - \mu_{\hat{\theta}}^{\text{boot}})$$

Experiments – Synthetic images (a recipe)

Take a region of Lena, shift randomly, add noise, and register.
Repeat $1000 \times$ for each noise type (3) and level (10).

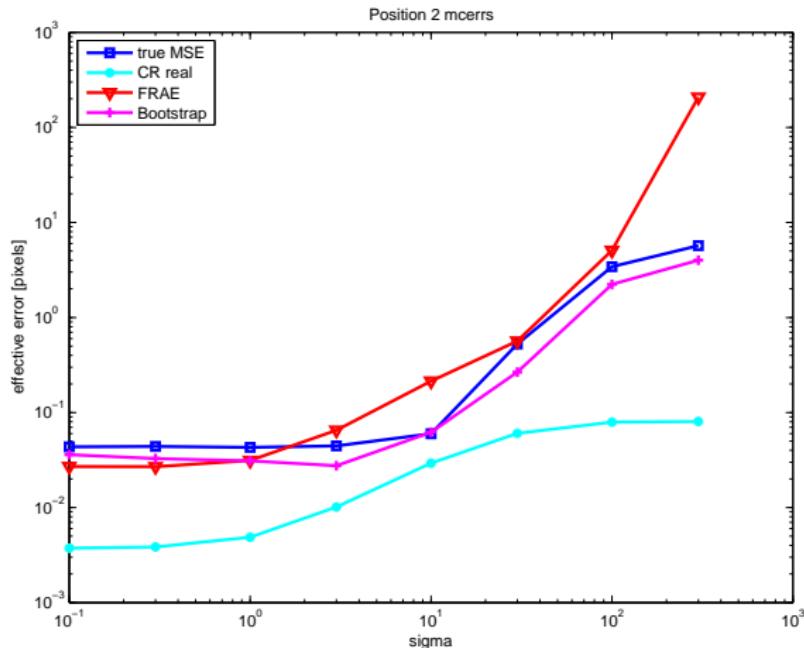


Bootstrap vs. FRAE vs. Cramér-Rao



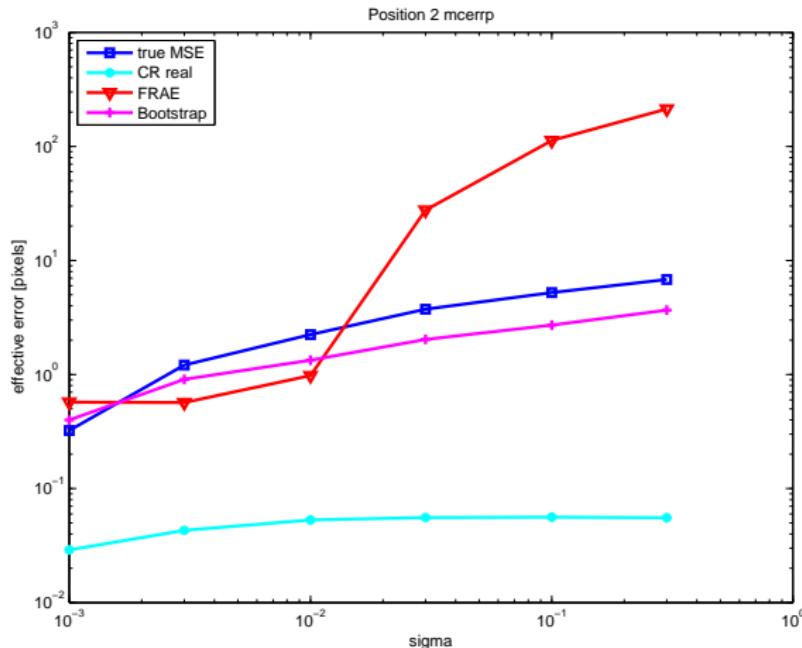
Position 2 (medium level of detail), white noise

Bootstrap vs. FRAE vs. Cramér-Rao



Position 2 (medium level of detail), correlated white noise

Bootstrap vs. FRAE vs. Cramér-Rao

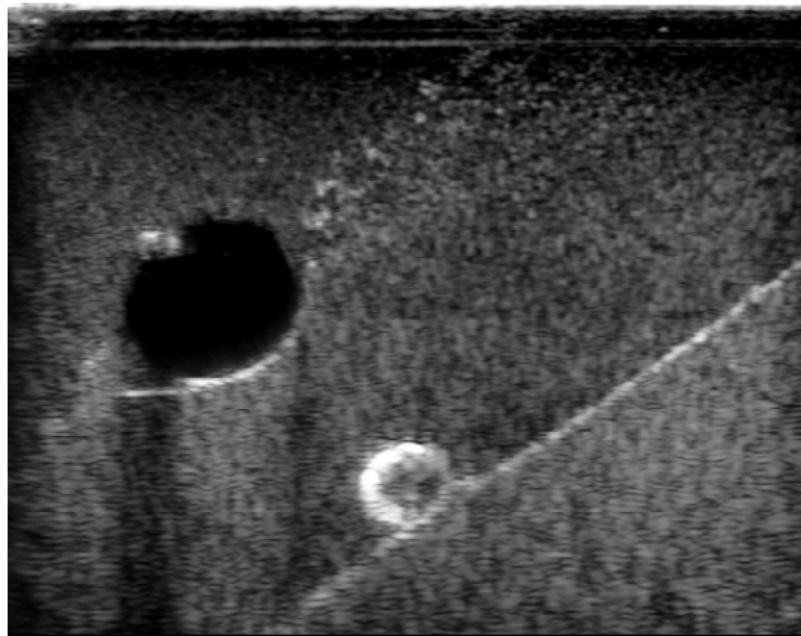


Position 2 (medium level of detail), salt&pepper noise

Spatial dependency

(low noise case, $\sigma = 3$)

Images to register (ultrasound)

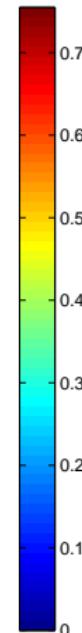
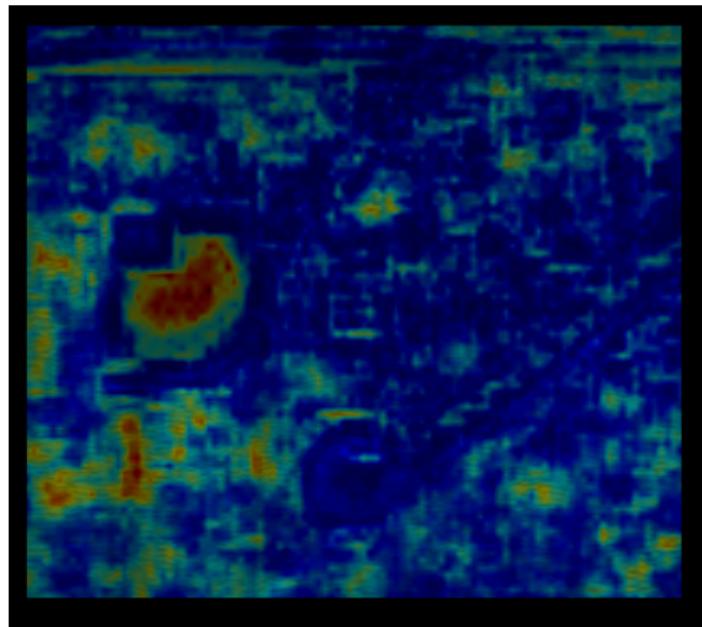


Red — high accuracy, Green — low accuracy.

Spatial dependency

(low noise case, $\sigma = 3$)

True mean square registration error

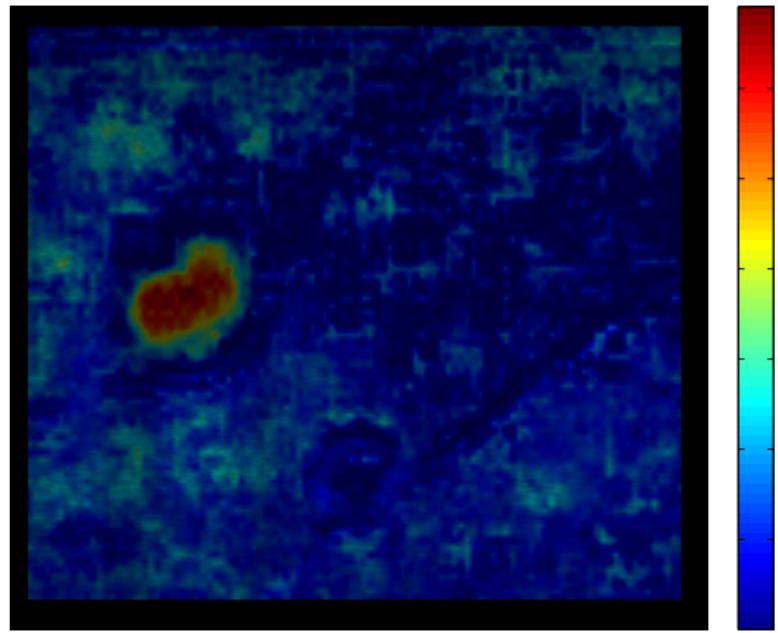


Red — high accuracy, Green — low accuracy.

Spatial dependency

(low noise case, $\sigma = 3$)

Estimate of the registration error (bootstrap)



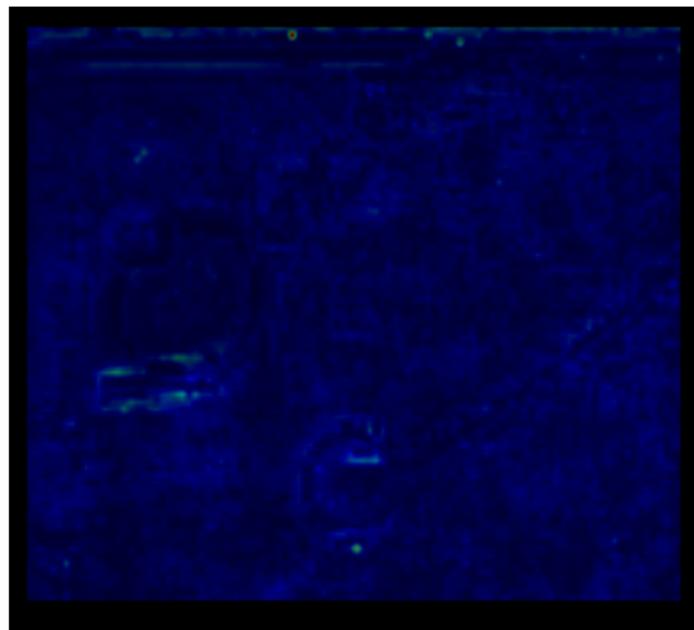
max MSE
6.0 pixels

Red — high accuracy, Green — low accuracy.

Spatial dependency

(low noise case, $\sigma = 3$)

Estimate of the registration error (FRAE)



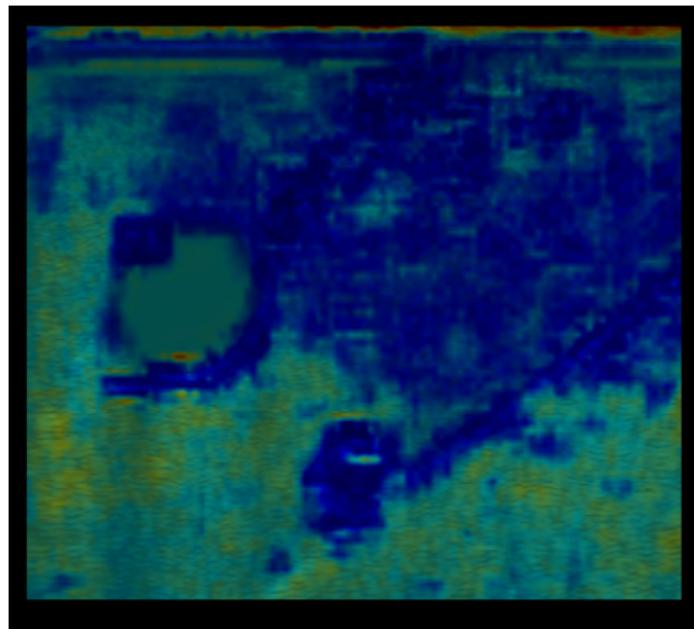
max MSE
527 pixels

Red — high accuracy, Green — low accuracy.

Spatial dependency

(low noise case, $\sigma = 3$)

Estimate of the registration error (Cramér-Rao)



max MSE
0.18 pixels

Red — high accuracy, Green — low accuracy.

Conclusions

(The End...)

- ▶ Estimate registration accuracy from input images only.
- ▶ Results on synthetic data:
 - ▶ FRAE — fast (seconds), often less accurate than bootstrap.
 - ▶ Bootstrap — slower (minutes), general, mostly accurate.
 - ▶ Cramér-Rao method — fast, significantly worse accuracy.
- ▶ Many (future) applications
- ▶ Results on real data: evaluation difficult, more work needed.

Závěr

- ▶ **Co nabízíme** Expertiza v oblasti
 - ▶ Zpracování a analýzy obrazů
 - ▶ Segmentace, registrace, předzpracování
 - ▶ Detekce, klasifikace, rozpoznávání, rekonstrukce

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