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# Optimization and Identification in Hyperthermia Treatment Planning

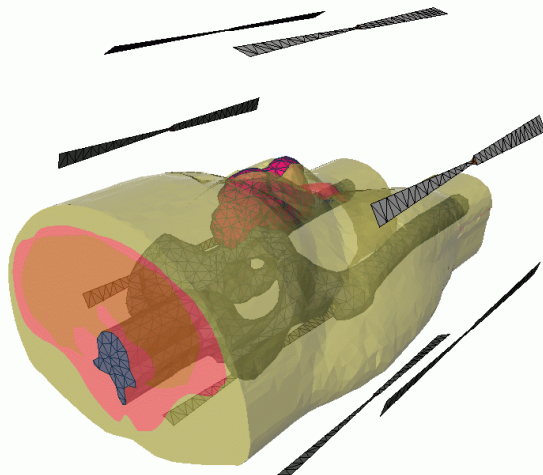
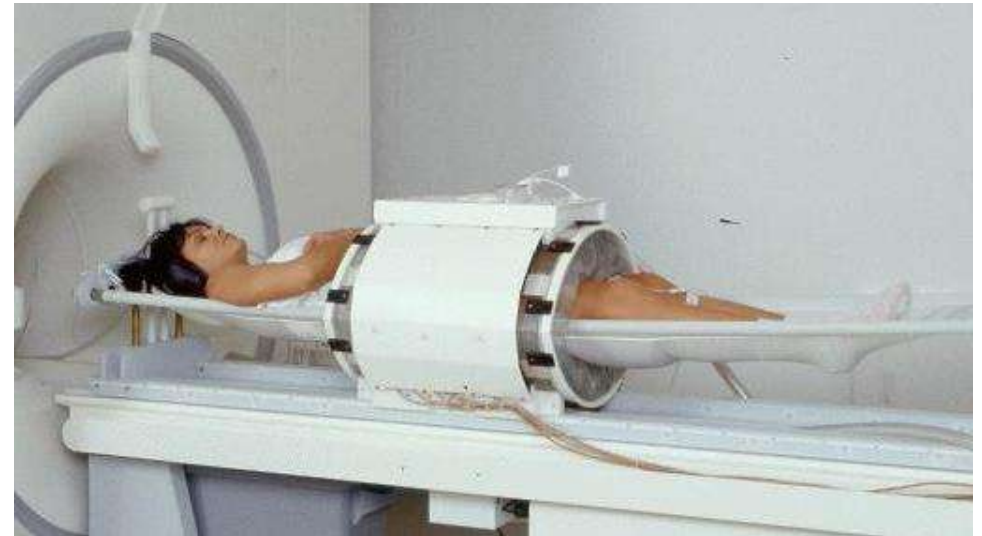
Aspects in Interior Point Methods for Optimal Control

## Principle

- tumors are susceptible to heat
- support radio- or chemotherapy by heating tumors

## Technology for Regional Hyperthermia

- phased array microwave radiation
- ultrasound
- magnetic nanoparticle fluids



## Mathematical Modelling

- virtual patient models
- Maxwell's equations / elastoacoustics
- bio-heat-transfer equation

## Optimization Task

Find a control  $u \in \mathbb{C}^{12}$  that optimizes the therapy.

cost functional  $\min J(T|_{\text{tumor}})$

state equations 
$$-\operatorname{div}(\kappa \nabla T) + c W(T)(T - T_a) = \frac{\sigma}{2} |E|^2$$

$$\kappa \partial_n T = h(T_{\text{out}} - T)$$

BHTE

$$\operatorname{curl} \frac{1}{\mu} \operatorname{curl} E = \omega^2 \epsilon E - i \omega J(u)$$

time-harmonic  
Maxwell's equations

constraints 
$$T|_{\text{healthy}} \leq T_{\text{max}}$$

$$\min \{|u_i|\} \geq \alpha \max \{|u_i|\}$$

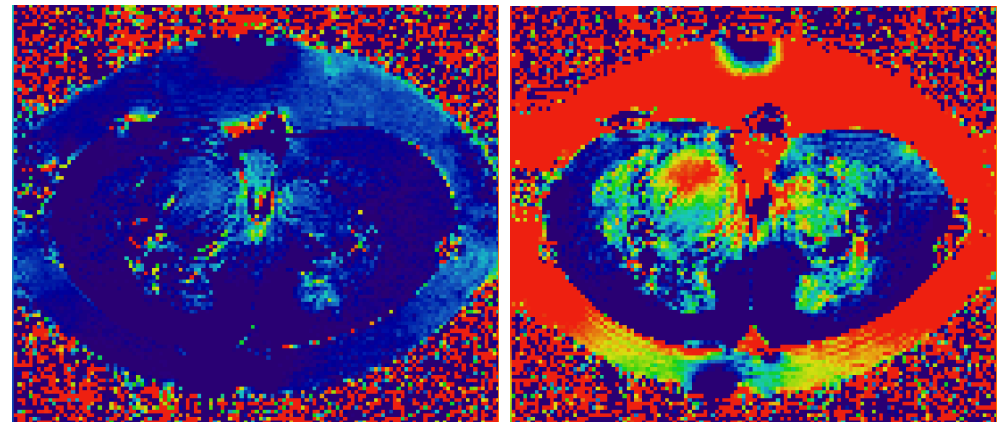
- fixed control setting: finite dimensional control  $u \in \mathbb{C}^{12}$
- periodic control setting: distributed control  $u \in L_\infty^{12}(0, \pi)$

## Sources of planning error

- individual and varying **perfusion**
- patient positioning
- generator and transmitter drift
- modelling errors
- material parameters
- numerical approximation errors

Is the therapy plan realized in practice?  
online MR “temperature” measurements

$$m = a(T - T_{\text{bas}}) + b(W - W_{\text{bas}}) + \delta$$



- noisy
- only partially available
- coefficients  $a$  and  $b$  not exactly known

## Parameter identification

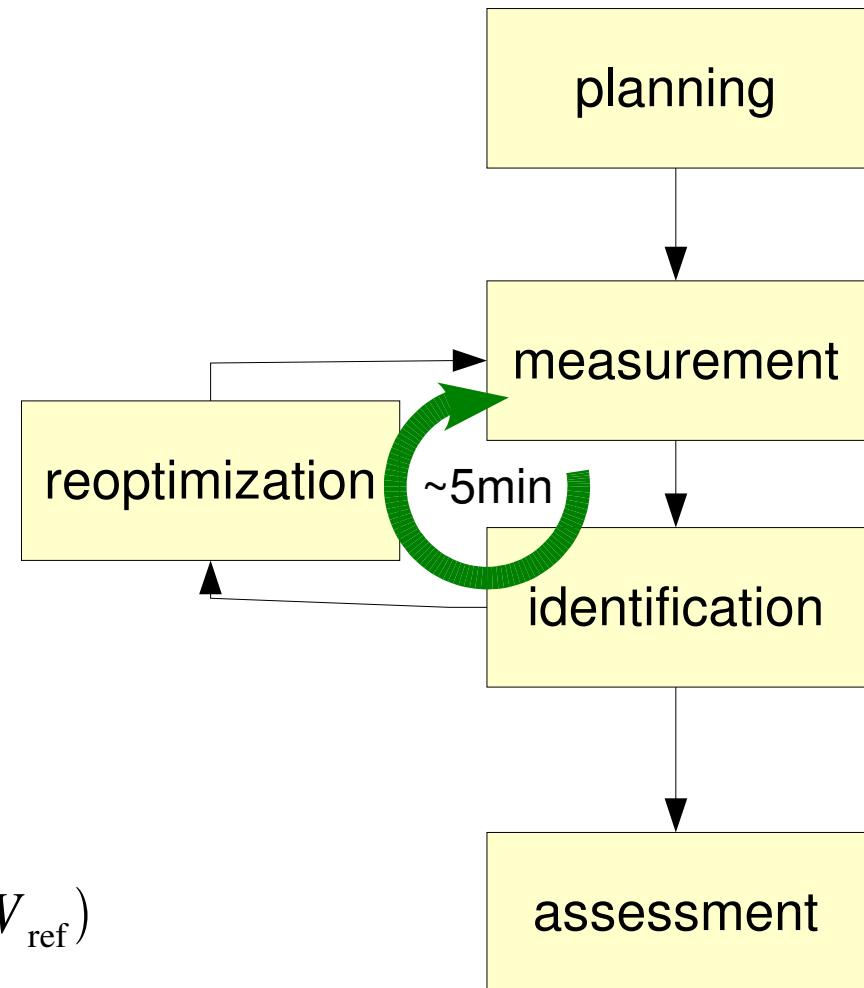
$$\min_{T, W} \frac{1}{2} \|m - a(T - T_{\text{bas}}) - b(W - W_{\text{bas}})\|^2 + \frac{\alpha}{2} \|W - W_{\text{ref}}\|^2 + \frac{\beta}{2} \sum_i \|\nabla(W - W_{\text{ref}})\|_{\Omega_i}^2$$

s.t. BHTE,  $W \geq 0$

## Sources of planning error

- individual and varying perfusion
- patient positioning
- generator and transmitter drift
- modelling errors
- material parameters
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## Online reoptimization of therapy



## Parametric sensitivities

sensitivity  $\partial_W u_{\text{opt}}$

update  $u_{\text{opt}}(W) \approx u_{\text{ref}} + \partial_W u_{\text{opt}}(W - W_{\text{ref}})$

Model problem  $\min_{u \in L^\infty, y \in H_0^1 \cap L^\infty} \frac{1}{2} \|y - y_d\|_{L_2}^2 + \frac{\alpha}{2} \|u\|_{L_2}^2$

subject to  $Ly + u = 0$

$$-1 \leq u \leq 1$$

IP regularization  $\min_{u \in L^\infty, y \in H_0^1 \cap L^\infty} \frac{1}{2} \|y - y_d\|_{L_2}^2 + \frac{\alpha}{2} \|u\|_{L_2}^2 - \mu \int_{\Omega} \ln(1+u) + \ln(1-u)$

subject to  $Ly + u = 0$

Homotopy  $\mu \rightarrow 0$

$$\|u(\mu) - u(0)\|_{\infty} \leq \sqrt{\mu}$$

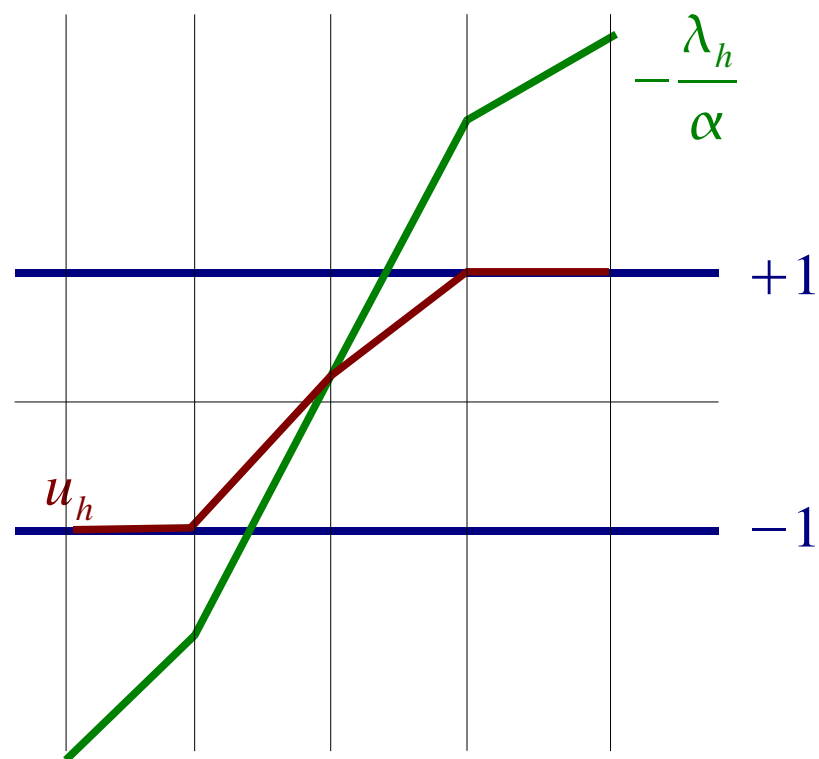
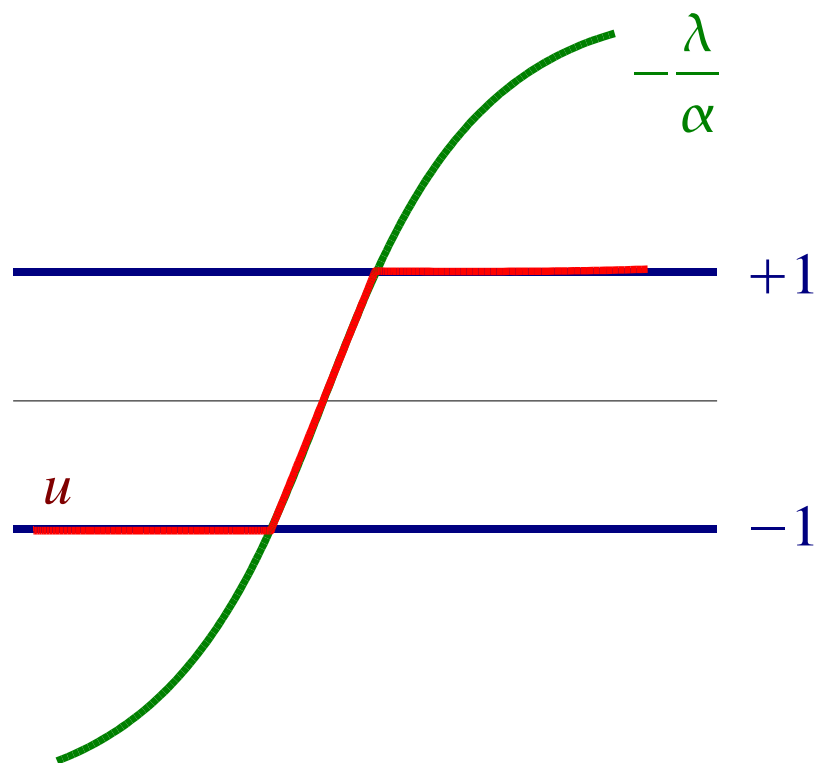
Classical (inexact) continuation

$$\mu_{k+1} \leq \sigma \mu_k \text{ linear convergence}$$

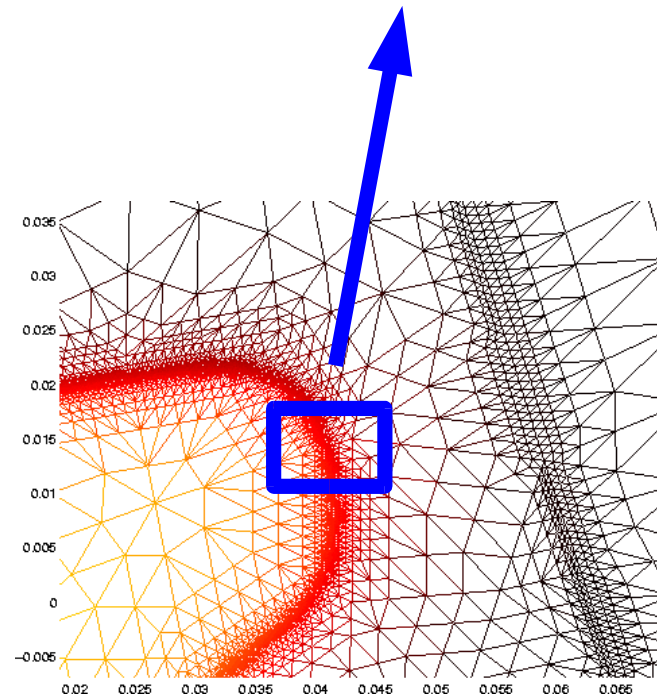
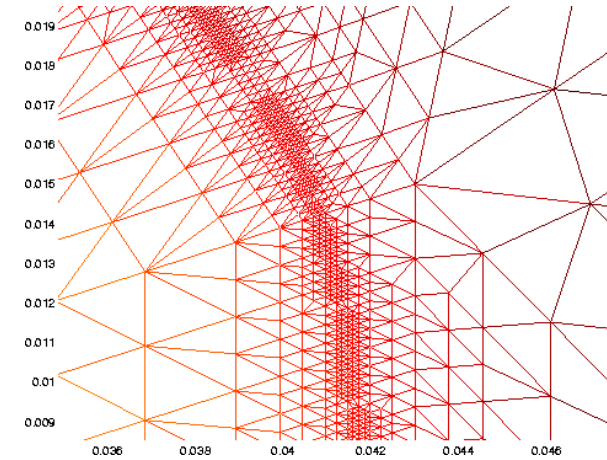
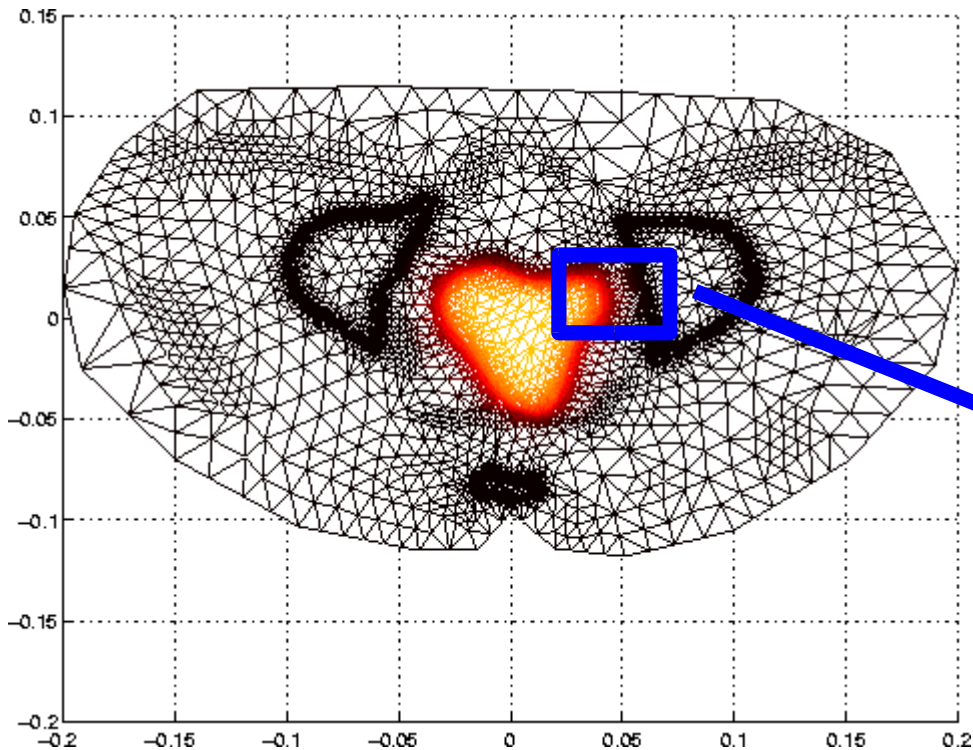
Projection formula  $y - y_d + Ly = 0$

$$u = \text{Proj}_{[-1,1]} -\frac{\lambda}{\alpha}$$

$$Ly + u = 0$$

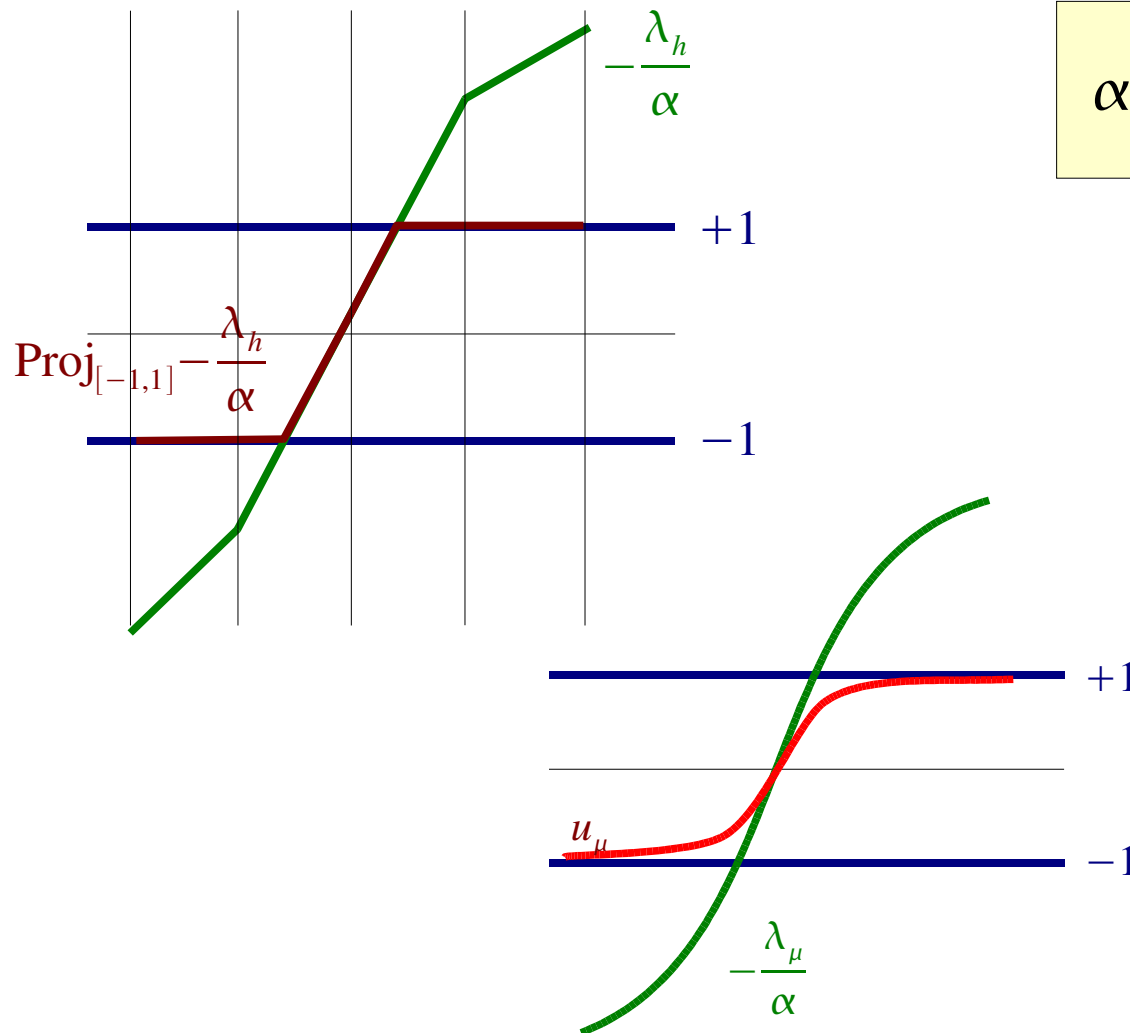


Accurate representation of control necessitates massive grid refinement at boundary of active set.





## Pointwise elimination of control



## IPM equivalent

$$y - y_d + L\lambda = 0$$

$$\alpha u + \lambda - \frac{\mu}{1-u} + \frac{\mu}{1+u} = 0$$

$$Ly + u = 0$$

$$1+u, 1-u \geq 0$$



$$y - y_d + L\lambda = 0$$

$$Ly + u(\lambda; \mu) = 0$$

$u(\lambda; \mu)$  solution of cubic equation

triangulation of  $\Omega$ :

$\mathbf{T}$   $\partial\Omega$  smooth

piecewise polynomial functions:

$$\mathbf{P}_{p,h} = \{\phi \in L^2 : \phi|_T \in \mathbf{P}_p \forall T \in \mathbf{T}\}$$

ansatz space:

$$V_h^p = \mathbf{P}_{p,h} \cap H_0^1 \quad p=1,2$$

weak formulation:

$$\begin{aligned} \langle y_h - y_d + L\lambda_h, \phi \rangle &= 0 \\ \langle Ly_h - P_h u(\lambda_h), \phi \rangle &= 0 \end{aligned} \quad \forall \phi \in V_h^p$$

exact integration

numerical integration:

linear projector  $P_h$

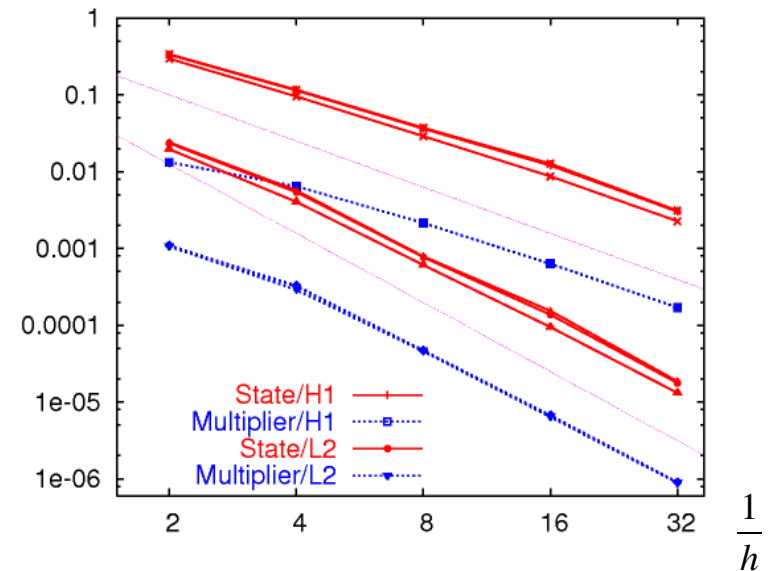
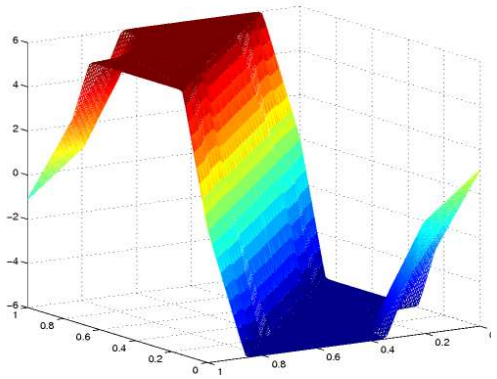
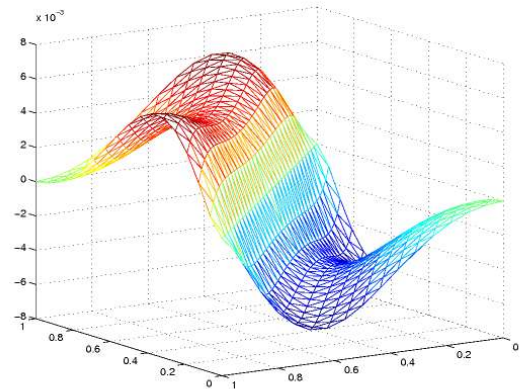
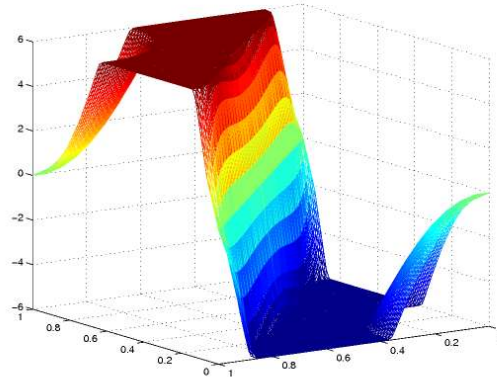
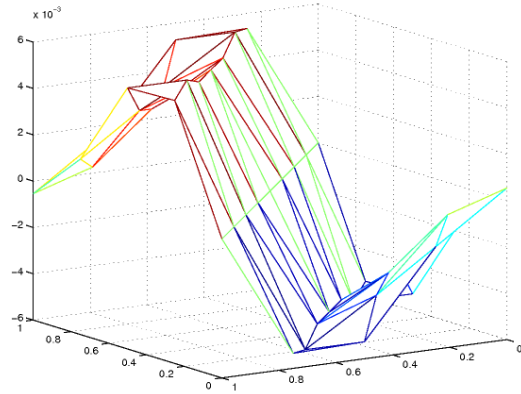
$$\|P_h u - u\|_{L^2} \leq c h^p \sqrt{\mu} \|u\|_{H^2, \mathbf{T}}$$

**Result:**

$$\|(y, \lambda)_h - (y, \lambda)(\mu)\|_{H^1} \leq c h^p \quad \|(y, \lambda)_h - (y, \lambda)(0)\|_{H^1} \leq c h^p$$

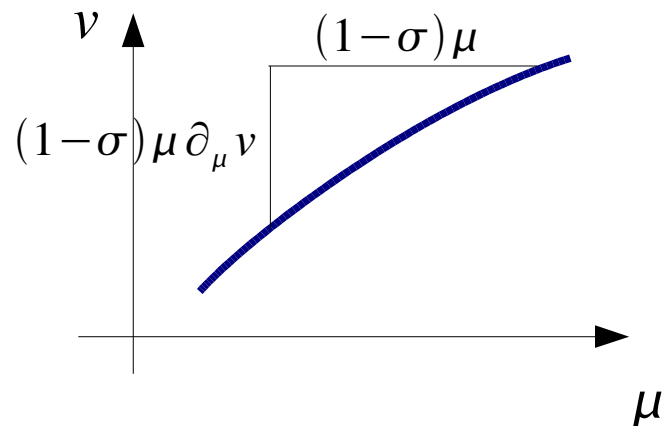
$$\|u_h - u(\mu)\|_{L^2} \leq c h^{p+1} \quad \|u_h - u(0)\|_{L^2} \leq c h^p$$

## High accuracy on coarse grids



Superlinear convergence

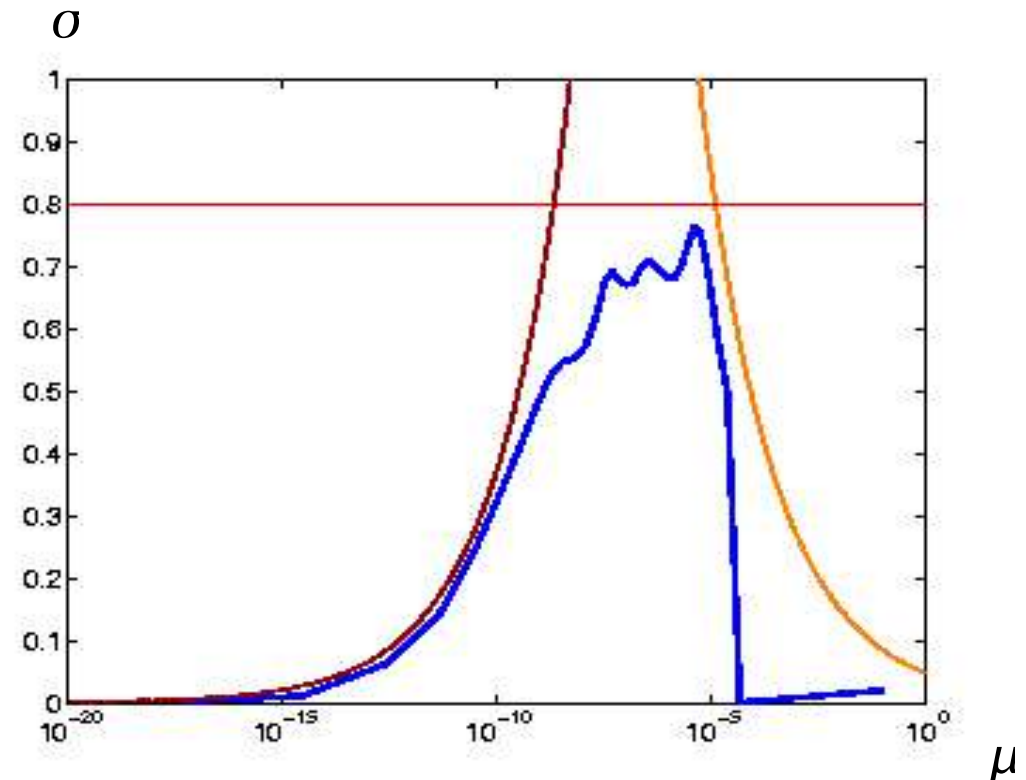
classical continuation



stepsize  $\sigma$  depends on

- slope of central path
- convergence radius of Newton corrector

$$\sigma(\mu) = O(-\mu^2 \ln \mu)$$



Control reduction not always possible

e.g. identification problem

$$J = \frac{1}{2} \|y - y_d\|^2 + \frac{\alpha}{2} \|u\|^2 + \frac{\beta}{2} \|\nabla u\|^2$$

$$Ly + u = 0, \quad u \geq 0$$

IP optimality system

$$y - y_d + L\lambda = 0$$

$$\alpha u - \Delta u + \lambda + \frac{\mu}{u} = 0$$

$$Ly + u = 0$$

$$u \geq 0$$

Control discretization

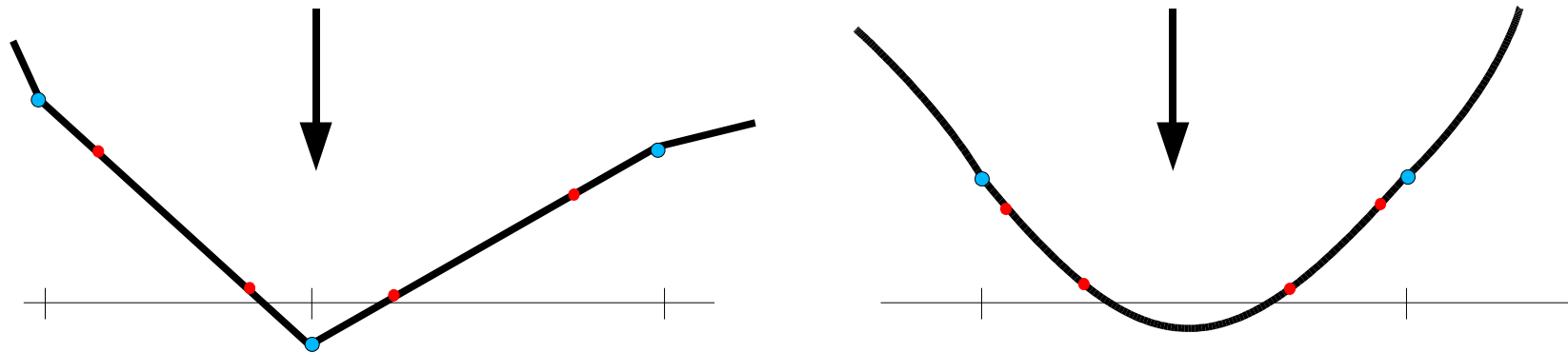
$$u_h \in \mathbf{P}_{p,h} = \{u : u|_T \in \mathbf{P}_p \quad \forall T \in \mathbf{T}\}$$

## Quadrature rules

assembly of barrier functional  $\int_{\Omega} \ln u(x) dx = \sum_T \int_T \ln u(x) dx$

$$\int_T \ln u(x) dx \approx \sum_i w_i \ln u(x_i)$$

- **discrete** barrier functional: only  $u(x_i) \geq 0$
- **linear** elements & linear constraints: use Lobatto quadrature  $u(x) \geq 0 \forall x$
- higher order elements:
  - perform **feasibility check** for Newton stepsize damping **at integration points only** or
  - perform **mesh refinement**



## Exact integration

instead of  $\int_T \ln u(x) dx \approx \int_T p(x) dx$  with  $p(x_i) = \ln u(x_i)$

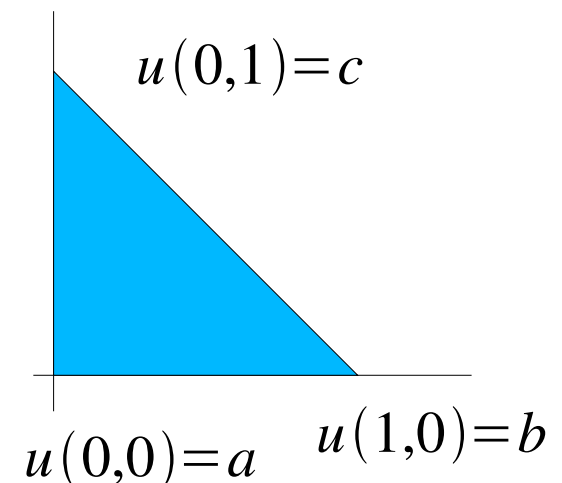
do  $\int_T \ln u(x) dx \approx \int_T \ln q(x) dx$  with  $q(x_i) = u(x_i)$

here:  $u|_T \in P$  allows for **exact** integration

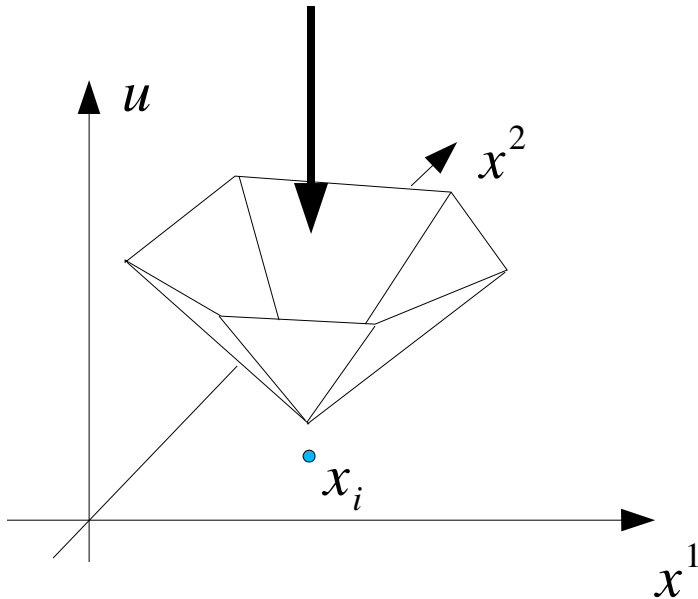
## Example: linear 2D elements

$$\int_T \ln u(x) dx = \frac{1}{c-a} \left( \frac{F(b)-F(c)}{b-c} + \frac{F(b)-F(a)}{b-a} \right)$$

$$F(z) = \frac{z^2}{2} \left( \ln z - \frac{3}{2} \right)$$



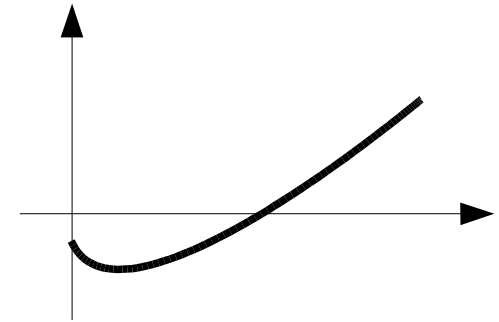
## Newton damping with exact integration



$$-\int_{T \ni x_i} \ln u(x) \, dx \approx -u(x_i) \ln u(x_i) =: f(u(x_i))$$

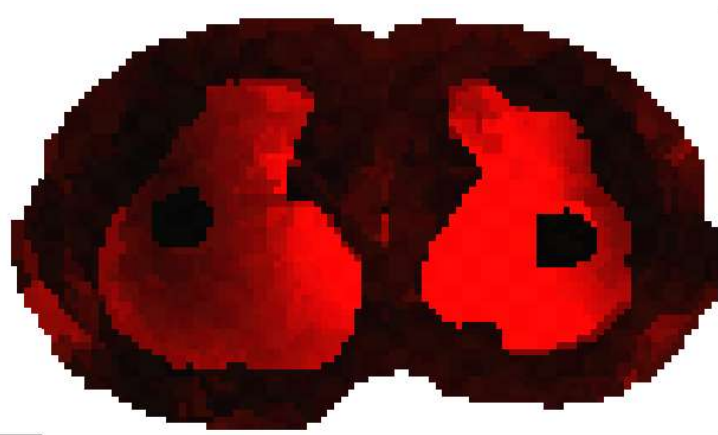
$$z \rightarrow 0: f(z) \rightarrow \text{const}$$

$$f'(z) \rightarrow -\text{const}$$

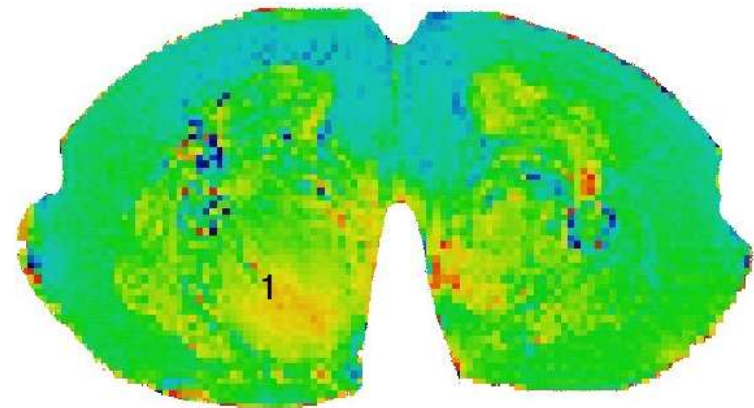


- **discrete** “barrier” functional need not have unconstrained minimizer
- **mesh refinement necessary**
- provides refinement criterion

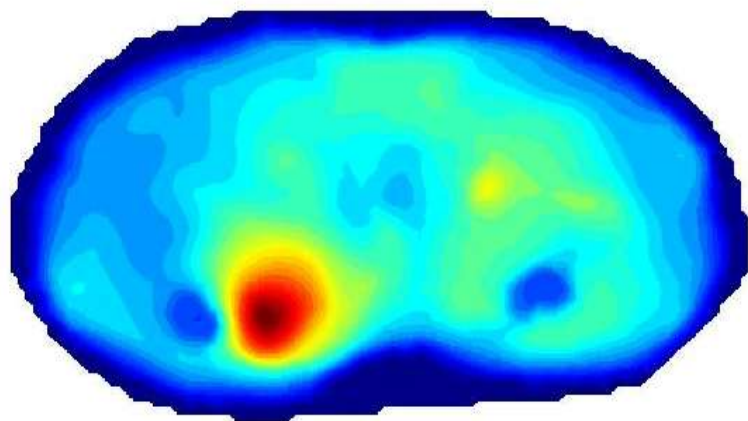




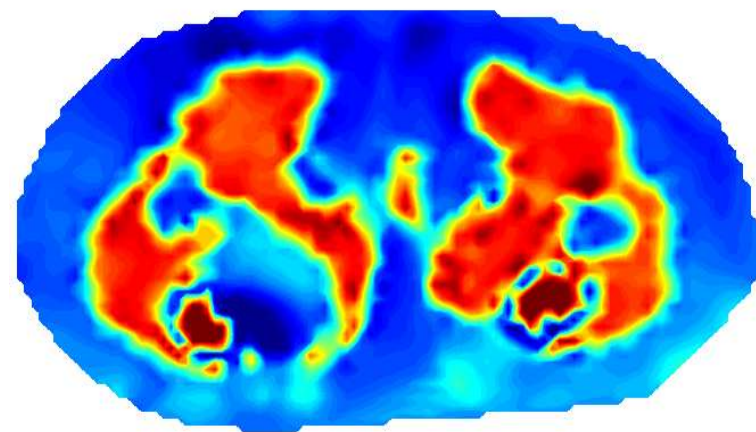
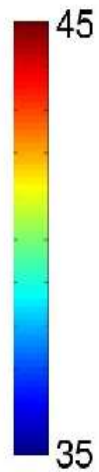
planning SAR



MR measurements



identified temperature



identified perfusion

## Model Problem

$$\min J(u; p) \quad \text{s.t. } u \geq \underline{u}$$

$$J(u; p) = \frac{1}{2} \langle u, K(p)u + l \rangle + \frac{\alpha}{2} \|u\|^2$$

## Parametric Sensitivity

$$u(p + \delta p) = u(p) + u_p(p) \delta p + o(\delta p)$$

$$\min_{u_p, \delta p} \langle u_p \delta p, J_{uu}(u; p) u_p \delta p + J_{up} \delta p \rangle$$

$$\text{s.t. } u_p = 0, \quad \eta > 0$$

$$u_p \geq 0, \quad \eta = 0, u - \underline{u} = 0$$

## IP Approximation

$$\min J(u; p) - \mu \int_{\Omega} \ln(u - \underline{u})$$

$$\text{gradient: } F(u; p, \mu)$$

## IP Sensitivity

$$u(p + \delta p, \mu) = u(p, \mu) + u_p(p, \mu) \delta p + o(\delta p)$$

$$u_p(p, \mu) = -F_u(u(p, \mu); p, \mu)^{-1} F_p(u(p, \mu); p, \mu)$$

Convergence

$$\min \int_{-1}^1 (u - x - p)^2 \quad \text{s.t. } u \geq 0$$

solution

$$\|u(p, \mu) - u(p)\|_{L_q} \leq c \mu^{(1+q)/2q}$$

$$q=2: \mu^{3/4}$$

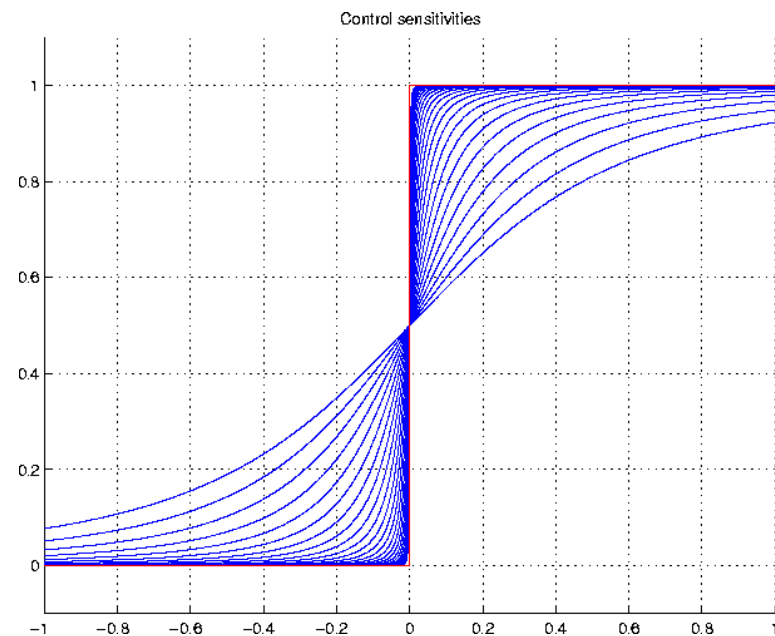
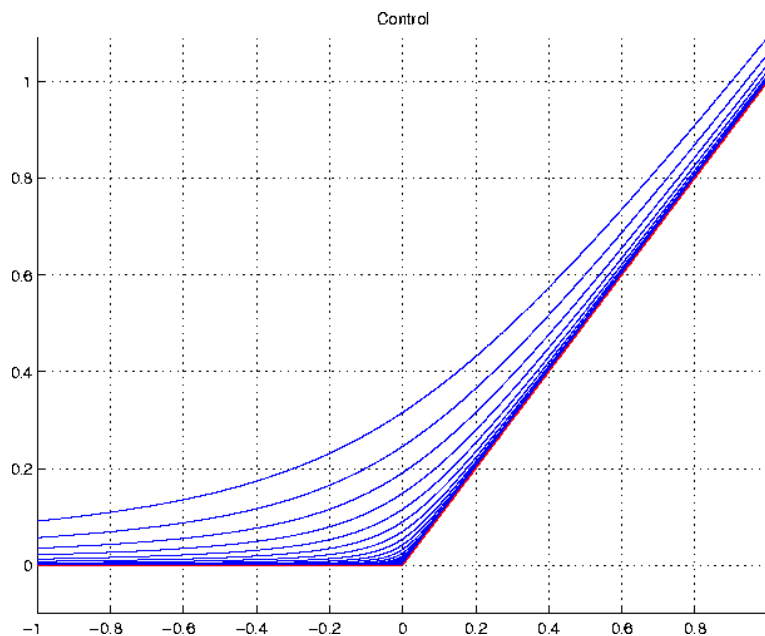
$$q=\infty: \mu^{1/2}$$

sensitivity

$$\|u_p(p, \mu) - u_p(p)\|_{L_q} \leq c \mu^{1/2q}$$

$$q=2: \mu^{1/4}$$

$$q=\infty: 1$$



... the collaborators:

- Anton Schiela, Tobias Gänzler, Peter Deuffhard (ZIB & MATHEON)
- Fredi Tröltzsch, Uwe Prüfert (TUB & MATHEON)
- Stefan Volkwein (Uni Graz)
- Roland Griesse (RICAM Linz)
- Peter Wust, Johanna Gellermann (Charité Berlin)

... you for your attention!

