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Otmar Scherzer
Editor

Mathematical Models for Registration and Applications to Medical Imaging

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Mathematical Models for Registration and Applications to Medical Imaging

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Editor

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Preface

Image registration is an emerging topic in image processing with many applications in medical imaging, picture and movie processing. The classical problem of image registration is concerned with finding an appropriate transformation between two data sets. This fuzzy definition of registration requires a mathematical modeling and in particular a mathematical specification of the terms *appropriate* transformations and *correlation* between data sets. Depending on the type of application, typically Euler, rigid, plastic, elastic deformations are considered. The variety of similarity measures ranges from a simple L^p distance between the pixel values of the data to mutual information or entropy distances.

This goal of this book is to highlight by some experts in industry and medicine relevant and emerging image registration applications and to show new emerging mathematical technologies in these areas.

Currently, many registration application are solved based on variational principle requiring sophisticated analysis, such as calculus of variations and the theory of partial differential equations, to name but a few. Due to the numerical complexity of registration problems efficient numerical realization are required. Concepts like multi-level solver for partial differential equations, non-convex optimization, and so on play an important role. Mathematical and numerical issues in the area of registration are discussed by some of the experts in this volume.

Moreover, the importance of registration for industry and medical imaging is discussed from a medical doctor and from a manufacturer point of view.

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June, 2005 *Otmar Scherzer (Innsbruck)*

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Part I

Numerical Methods

A Generalized Image Registration Framework using Incomplete Image Information – with Applications to Lesion Mapping

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Abstract This paper presents a novel variational approach to obtain a d-dimensional displacement field $u = (u_1, \cdots, u_d)^t$, which matches two images with incomplete information. A suitable energy, which effectively measures the similarity between the images is proposed. An algorithm, which efficiently finds the displacement field by minimizing the associated energy is presented. In order to compensate the absence of image information, the approach is based on an energy minimizing interpolation of the displacement field into the holes of missing image data. This interpolation is computed via a gradient descent flow with respect to an auxiliary energy norm. This incorporates smoothness constraints into the displacement field. Applications of the presented technique include the registration of damaged histological sections and registration of brain lesions to a reference atlas. We conclude the paper by a number of examples of these applications.

Keywords image registration, inpainting, functional minimization, finite difference discretization, regularization, multi-scale

1 Introduction.

Deformable image registration of brain images has been an active topic of research in recent years. Driven by ever more powerful computers, image registration algorithms have become important tools, e.g. in

- guidance of surgery,
- diagnostics,
- quantitative analysis of brain structures (interhemispheric, interareal and interindividual),
- ontogenetic differences between cortical areas,
- interindividual brain studies.

The need for registration in interindividual brain studies arises from the fact that the human brain exhibits a high interindividual variability. While the topology is stable on the level of primary structures, not only the general shape, but also the spatial localization of brain structures varies considerably across brains. That renders a direct comparison impossible. Hence, brains have to be registered to a common “reference space”, i.e. they are registered to a reference brain. Often there are also, so-called maps, that reside in the same reference space. In so called brain atlases there are additional maps that contain different kinds of information about the reference brain, such as labeled cortical regions. Once an individual brain has been registered to the reference brain the maps can be transferred to the registered brain. It is not only that obtaining the information from the individual brain itself is often more intricate than registering it to a reference, in some cases it is also impossible. For instance, the microstructure of the brain cannot be analyzed in vivo, since the resolution of in vivo imaging methods, such as MRI and PET, is too low. Registration can also be a means of creating such maps, by transferring information from different brains into a reference space.

In the last decade computational algorithms have been developed in order to map two images, i.e. to determine a “best fit” between them. Although these techniques have been applied very successfully for both the uni- and the multi-modal case (e.g. see [1, 2, 7, 8, 10, 11, 13, 19, 21, 22, 25]) these techniques may be less appropriate for studies using brain-damaged subjects, since there is no compensation for the structural distortion introduced by a lesion (e.g. a tumor, ventricular enlargement, large regions of atypical pixel intensity values, etc.).

Generally the computed solution cannot be trusted in the area of a lesion. The magnitude of the effect on the solution depends on the character of the registration scheme employed. It is not only that these effects are undesirable, but also that in some cases one is especially interested in where the lesion would be in the other image. If, for instance, we want to know which function is usually performed by the damaged area, we could register the lesioned brain to an atlas and map the lesion to functional data within the reference space.

In more general terms the problem can be phrased as follows. Given are two images and a domain G including a segmentation of the lesions. The aim of the proposed image registration algorithm is to find a “smooth” displacement field, which

- minimizes a given similarity functional and
- conserve the lesion in the transformed template image.

There have been approaches to register lesions manually[12]. In this paper we present a novel automatically image registration approach for human brain volumes with structural distortions (e.g a lesion). The main idea is to define a suitable matching energy, which effectively measures the similarity between the images. Since the minimization solely the matching energy is an ill-posed problem we minimize the energy by a gradient descent flow with respect to a regularity energy borrowed from linear elasticity theory. The regularization energy incorporates smoothness constraints into the displacement field during the iteration.

The presented approach can be seen as the well known “image inpainting approach” (e.g. see [3, 5, 6]) for the unknown displacement field u. In inpainting missing or damaged parts of an image are restored using information from the surrounding area. Applications include the restoration of damaged photographs and movies or the removal of selected objects.

The analogy to image inpainting is given as follows: both approaches

1. consider a data model restricted on a domain $\Omega \setminus G$, where data is missing on G,
2. use a regularity energy defined on Ω,
3. determine a solution defined on Ω.

	Inpainting	proposed appr.
Input:	$I\|_{\Omega\setminus G}$	$T\|_{\Omega\setminus G_1}$,$R\|_{\Omega\setminus G_2}$
Data model:	restricted $\Omega \setminus G$	restricted $\Omega \setminus (G_1 \cup G_2)$
Regularity energy:	defined on Ω	defined on Ω
Output:	entire image $I\|_{\Omega}$	entire displacement field $u\|_{\Omega}$

The paper is organized as follows. In section 2 we describe an abstract mathematical framework to handle a variety of distance measures so-called matching energies. In the next section we present a novel variational approach, which matches two images with absent information on a part of the image-domain. The aim of the approach is to obtain a d-dimensional displacement field defined on Ω which preserves the lesion in the transformed images.

For this reason a suitable matching energy, which effectively measures the similarity between the images is proposed. Even when the images contain complete information, the sole minimization of the matching energy is an ill-posed problem. Thus, we add an auxiliary Lagrange term, given by an energy norm, which incorporates smoothness constraints into the displacement field.

In order to present a general description of the approach we use a general framework up to this point. In section 4 we present the numerical description, with a particular choice of the matching energy as well as for the energy norm for the displacement field. We discuss the discretization of the problem and the underlying numerical scheme to solve the resulting subproblems. In section 5 we present two- and three-dimensional results, where brain data is used. For the two-dimensional example we use a digitized histological section. In the three-dimensional case the approach is applied to lesioned MR volume data that is registered to a reference brain.

2 Abstract Framework.

Given are two images, a reference R and a template T using the same or different imaging modalities. We assume that in continuous variables the images can be represented by compactly supported functions

$$T, R : \varOmega \subset \mathbb{R}^d \to \mathbb{R}.$$

Usually, these images are two- or three-dimensional. This means, the map associates with each pixel (picture element)

$$x = (x_1, \cdots, x_d)^t$$

on the image domain $\varOmega$ its intensities $T(x)$ and $R(x)$. For the purpose of numerical computation $\varOmega$ will simply be the d-dimensional unit square $[0,1]^d$. We assume that T is distorted by an invertible deformation ϕ^{-1}. We search for a transformation

$$\phi(u)(\cdot) \;:\; \mathbb{R}^d \to \mathbb{R}^d, \quad \phi(u)(x) \;:\; x \mapsto (x_1 - u_1(x), \cdots, x_d - u_d(x))^t$$

that depends on the unknown displacements

$$u :\; \mathbb{R}^d \to \mathbb{R}^d, \quad u :\; x \mapsto u(x) := (u_1(x), \cdots, u_d(x))^t.$$

The goal of image registration is to determine $u(x)$ in such a way that the transformed template $T \circ \phi(u(x))$ matches the reference R. The image registration problem can be identified with a minimization problem in the following manner:

Problem 1. IMAGE REGISTRATION PROBLEM
For an energy functional

$$D[R, T, \varOmega;\; u(x)] := \int_{\varOmega} \varPhi(R, T, u)\; dx \;:\; \mathbb{R}^d \to \mathbb{R},$$

which measures the disparity between $T \circ \phi(u(x))$ and $R(x)$ on the image domain $\varOmega$, the image registration problem is given by the following minimization problem:

$$\text{Find } u(x), \text{such that } D[R, T, \varOmega;\; u(x)] \text{ is minimal.} \tag{1}$$

Thus we ask for solutions of the problem to minimize $D[R, T, \varOmega;\; u(x)]$ over

$$L_2^d(\varOmega) := \underbrace{L_2(\varOmega) \times \cdots \times L_2(\varOmega)}_{d-times}.$$

A minimizer $u(x)$ of (1) is characterized by the necessary condition

$$grad\big(D[R, T, u(x)]\big) = 0,$$

where $grad\big(D[R, T, u(x)]\big) \in L_2^d(\varOmega)$. Indeed, we require

$$\big\langle grad(D[R, T, u(x)]), \varphi \big\rangle = 0 \quad \forall \varphi \in L_2^d(\varOmega).$$

In the following we denote the so-called external forces $grad\big(D[R, T, u(x)]\big)$ just by $f(u(x))$. In the image registration process the task of the external forces is to bring similar regions of the images into correspondence. For instance, in the situation that the intensities of the given images are comparable, a common approach is to minimize their squared difference (see, e.g. [1, 2, 7, 13, 21]) for all $x \in \Omega$, i.e. to minimize

$$D_{SD}[R,T;\ u(x)] = \int_{\Omega} \Big(T(x_1 - u_1(x), \cdots, x_d - u_d(x)) - R(x_1, \cdots, x_d) \Big)^2 d\Omega. \tag{2}$$

It is used, for example, in the case that the images are recorded with the same imaging machinery, the so-called mono-modal image registration. The necessary condition for a minimizer $u^*(x)$ of (2) is given by:

$$\begin{aligned} f_{SD}(u(x)) = -grad\big(T(x_1 - u_1(x), \cdots, x_d - u_d(x))\big) \cdot \\ \big(T(x_1 - u_1(x), \cdots, x_d - u_d(x)) - R(x_1, \cdots, x_d)\big) \end{aligned}$$

see, e.g. [20].

Another kind of problem is the so-called multimodality image matching (see, e.g. [9, 22, 23, 26, 29]). Here, the distance between the images is measured by mutual information or entropy based functionals.

Recently, an approach based on the definition of a matching energy, which measures the local morphological "defect" between the images, has been presented [11].

Unfortunately, the image registration problem (1) is not well posed: Solutions, if they exist, are in general neither unique nor stable. Different solutions can give very similar outputs, and small data errors can yield very different solutions. Therefore, the approximations u of (1) may be useless. One has to define better approximate solutions. Since the problem is ill-posed, we have to apply a regularizing technique to solve the problem in a stable way. Many regularization methods are discussed in the literature and the choice of the regularization term depends crucially on the underlying application.

3 Gradient Descent Flow Using Incomplete Image Information.

The aim of this section is to determine a displacement field u on domains where the image information is unavailable.

3.1 Extension of the Similarity Functional

Let Ω denote the complete image domain for the image registration problem presented in the previous section. We assume that there are domains $U_i \subset \Omega$, $1 \leq i \leq s$, where image data in the template image T is missing respectively domains $V_j \subset \Omega, 1 \leq j \leq t$, where image data in the reference image R is missing.

Then the image registration problem is given by:

Problem 2. IMAGE REGISTRATION WITH INCOMPLETE INFORMATION
Let $G := G_U \cup G_V$ and $\Omega' = \Omega \setminus G$ an open domain, with

$$G_U = \left\{ x \in \mathbb{R}^d \;\middle|\; x \in \Omega \cap (U_1 \cup \cdots \cup U_s) \right\}$$

and

$$G_V = \left\{ x \in \mathbb{R}^d \;\middle|\; x \in \Omega \cap (V_1 \cup \cdots \cup V_t) \right\}.$$

Then the complete image registration problem for images with incomplete information is given by the following minimization problem:

$$\text{Find } u(x), \text{such that } D[R, T, \Omega';\; u] \text{ is minimal.} \tag{3}$$

In order to solve the problem we define an extension of the functional D as follows.

Definition 1. *The* **zero extension** $D_\epsilon[R, T, \Omega';\; u]$ *of the similarity function is defined by*

$$D_\epsilon[R, T, \Omega';\; u] := \int_{\Omega'} \Phi_\epsilon(R, T, u)\, dx,$$

with

$$\Phi_\epsilon(R, T, u) := \begin{cases} \Phi_\epsilon(R, T, u) & \text{if } x \in \Omega', \\ 0 & \text{if } x \in G. \end{cases}$$

With this definition we can restate problem 2.

Problem 3. MODIFIED IMAGE REGISTRATION PROBLEM
By using the zero extension of the similarity function $D_\epsilon[R, T, \Omega;\; u]$ the complete image registration problem for images with incomplete information is given by the following minimization problem:

$$\text{Find } u(x), \text{such that } D_\epsilon[R, T, \Omega;\; u] \text{ is minimal.} \tag{4}$$

We now describe an approach to solve the minimization problem. Because the problem is nonlinear, we have to use an iterative method. Assume that after k iterations a current deformation $\phi_k = x - u^{(k)}(x)$ is given, then the domains G and Ω'_k are changed in the following way

$$G_k = \phi_k\,(G_U) \cup G_V, \quad \Omega'_k = \Omega \setminus G_k,$$

since the displacements only acts on the template image.

3.2 Extended Iterative Minimization Method

To minimize $D_\epsilon[R,T,\Omega;\ u]$ for a given current approximation $u^{(k)}$, we search for an approximation $u^{(k+1)}$ so that

$$D_\epsilon[R,T,\Omega;\ u^{(k+1)}] < D_\epsilon[R,T,\Omega;\ u^{(k)}].$$

The reduction for the next iterate $u^{(k+1)}$ is given approximately by

$$D_\epsilon[R,T,\Omega;\ u^{(k+1)}] - D_\epsilon[R,T,\Omega;\ u^{(k)}] \approx \frac{\partial}{\partial d^{(k)}} D_\epsilon[R,T,\Omega;\ u^{(k)}], \qquad (5)$$

where the Gâtaux-derivative at $u^{(k)}$ in the descend direction

$$d^{(k)} = u^{(k+1)} - u^{(k)}$$

is given by

$$\frac{\partial}{\partial d^{(k)}} D_\epsilon[R,T,\Omega;\ u^{(k)}] = \left\langle f_k, d^{(k)} \right\rangle_{L_2(\Omega)}$$

with

$$f_k := f(u^{(k)}) = \begin{cases} grad(D_\epsilon[R,T,\Omega;\ u^{(k)}]) & \text{if } x \in \Omega_k', \\ 0 & \text{if } x \in G_k. \end{cases}$$

By using the negative gradient the nonlinear steepest descent iteration for problem 3 is given by

$$u^{(k+1)} = u^{(k)} - \tau_k f_k, \qquad (6)$$

with

$$\tau_k = \arg\min_{\tau \in \mathbb{R}} D_\epsilon[R,T,\Omega;\ u^{(k)} - \tau f_k].$$

Unfortunately, for most real applications the steepest descent iteration (6) is not suitable to solve the image registration problem. This is at least due to two factors. First, because of the ill-posedness, this method does not have global convergence properties. Second, due to noise sensitivity of the ill-posed registration problem, regularization techniques have to be applied in order to compute meaningful solutions. Hence, to ensure robustness and fast local convergence it is necessary to incorporate additional information.

3.3 Filling-in by an Unified Regularization Approach

A natural way to alleviate this effects is to find a descend direction subject to an energy constraint $||\cdot||_E$ smaller than some particular value η, i.e.

$$\arg\min \left\langle f_k, d^{(k)} \right\rangle_{L_2(\Omega)}, \quad \text{s.t.} \quad ||d^{(k)}||_E^2 \le \eta,$$

where the energy norm $||\cdot||_E$ is defined by

$$||v||_E = \sqrt{\langle v, v \rangle_E}$$

with inner product

$$\langle v, w \rangle_E = \langle Lv, w \rangle_{L_2^d(\Omega)}$$

and a symmetric positive definite operator L.

Remark 1. In order to guarantee positive definiteness of the operator L in the following, we assume Dirichlet boundary conditions, i.e.

$$d^{(k)}(x) = 0 \quad \text{for} \quad x \in \partial\Omega \quad \text{and} \quad k = 0, 1, 2, \cdots .$$

Other possibilities to guarantee positive definiteness are described in cf. [17].

The method of Lagrange multipliers gives the functional

$$\arg\min_{d^{(k)}} \left\{ \left\langle f_k, d^{(k)} \right\rangle_{L_2(\Omega)} + \alpha \left\langle Ld^{(k)}, d^{(k)} \right\rangle_{L_2(\Omega)} \right\}, \tag{7}$$

with some parameter $\alpha(\eta) = \alpha > 0$. We have the following result:

Theorem 1. *The unique minimizer of (7) is characterized by the following boundary value problem*

$$\left.\begin{array}{ll} \alpha L\, d^{(k)}(x) = -grad(D_\epsilon[R, T, \Omega;\ u^{(k)}]) & \textit{for } x \in \Omega'_k, \\ \alpha L\, d^{(k)}(x) = 0 & \textit{for } x \in G_k, \\ d^{(k)}(x) = 0 & \textit{for } x \in \partial\Omega. \end{array}\right\} \tag{8}$$

Proof. Since L is a symmetric positive definite operator, a weak solution of (7) is given by the variational equation

$$\left\langle \alpha L d^{(k)}, \varphi \right\rangle_{L_2(\Omega)} = \langle -f_k, \varphi \rangle_{L_2(\Omega)} \tag{9}$$

for every φ with $\varphi = 0$ on $\partial\Omega$. Classical solutions fulfill

$$\begin{array}{ll} \alpha L\, d^{(k)}(x) = -f_k & \text{for } x \in \Omega, \\ d^{(k)}(x) = 0 & \text{for } x \in \partial\Omega \end{array}$$

or equivalent

$$\begin{array}{ll} \alpha L\, d^{(k)}(x) = -grad(D_\epsilon[R, T, \Omega;\ u^{(k)}]) & \text{for } x \in \Omega'_k, \\ \alpha L\, d^{(k)}(x) = 0 & \text{for } x \in G_k, \\ d^{(k)}(x) = 0 & \text{for } x \in \partial\Omega. \end{array}$$

□

We minimize $D_\epsilon[R, T, \Omega;\ u]$ by successively determining $d^{(k)} = -\alpha^{-1} L^{-1} f_k$ as solution of (8) and perform the following iteration

$$u^{(k+1)} = u^{(k)} + d^{(k)} = u^{(k)} - \alpha^{-1} L^{-1} f_k \text{ for } k = 0, 1, \ldots$$

with an initial guess $u^{(0)}(x) = u^*(x)$ and $u^{(k+1)}(x) = 0$ for $x \in \partial\Omega$. If in each iteration step the scalar α^{-1} is chosen to minimize

$$\tau_k = \arg \min_{\alpha^{-1}\in\mathbb{R}} D_\epsilon[R, T, \Omega;\ u^{(k)} - \alpha^{-1}L^{-1}f_k],$$

then one obtains the steepest descent method with respect to the energy $||\cdot||_E^2$. If one restricts the parameter $\alpha^{-1} \in [0, 2||d^{(k)}||_\infty^{-1}]$, i.e.

$$\begin{aligned}\tau_k &= \arg \min_{\alpha^{-1}\in[0,2||d^{(k)}||_\infty^{-1}]} D_\epsilon[R, T, \Omega;\ u^{(k)} - \alpha^{-1}L^{-1}f_k] \\ &= \arg \min_{\alpha^{-1}\in[0,2]} D_\epsilon[R, T, \Omega;\ u^{(k)} - \alpha^{-1}L^{-1}f_k||d^{(k)}||_\infty^{-1}] \qquad (10)\end{aligned}$$

one obtains a method known as Landweber iteration with trust-region restriction. This means that the template image is moved in one iteration step by at most two pixels. In practice, this seems to be a reasonable compromise between convergence speed and robustness. We stop the iteration when $grad\big(D_\epsilon[R, T, \Omega;\ u^{(k)}]\big) \approx 0$ and get algorithm 1.

Algorithm 1 Iterative minimization of $D_\epsilon[R, T, \Omega;\ u]$

$k = 0$; $u^{(0)} = 0$;
repeat
  calculate $f(u^{(k)}(x))$ on $\Omega'_k = \Omega \setminus G_k$
  compute $d^{(k)}$ from *(8)*
  set $s^{(k)} = d^{(k)}/||d^{(k)}||_\infty$
  compute τ_k by solving problem *(10)*
  set $u^{(k+1)} = u^{(k)} + \tau_k \cdot s^{(k)}$
  set $k = k + 1$
  compute $G_k = \phi_k(G_U) \cup G_V$
until $||f(u^{(k)}(x))||^2 \leq eps$

Remark 2. In some applications it is useful to determine a descend direction subject to a semi-norm. Then the operator L is only positive semi-definite and consequently the operator contains a non-trivial kernel. In this situation one has to consider the following situations:

1. If $f_k \notin (L)$ then
$$\tilde{d}^{(k)} = L^+ f_k$$
is the least squares solution of (8).
2. If $f_k \in (L)$ then all solutions of (8) are given by $d^{(k)} = \tilde{d}^{(k)} + v\lambda$, where $\lambda \in \mathbb{R}^d$ and v is an arbitrary basis for $ker(L)$.

In the second case the parameter λ is chosen to minimize

$$D_\epsilon[R, T, \Omega;\ u^{(k+1)} - \lambda v]$$

in each iteration.

4 Algorithmic Aspects

In this section we will turn to the numerical aspects of the proposed approach. We present an algorithm for the efficient and robust computation of solutions $d^{(k)}$ of (8).

4.1 Model

For our specific application we choose

$$D_\epsilon[T, R, \Omega; u] := \frac{1}{2} \int_{\Omega'} (T(x - u(x)) - R(x))^2 \mathrm{d}x \tag{11}$$

as the energy functional, i.e. the least squared difference. For the regularization term $\langle Lu, u \rangle$ we chose the elliptic differential Navier-Lamé operator

$$Lu := -\mu \Delta u - (\mu + \lambda) \nabla(\nabla u), \tag{12}$$

with Dirichlet boundary conditions, i.e. $u = 0$ for $x \in \Gamma$. The "external force" is then given by

$$f(u(x)) = \begin{cases} -\nabla T(x - u(x)) \left(T(x - u(x)) - R(x)\right) & , x \in \Omega' \\ 0 & , \text{otherwise} \end{cases} . \tag{13}$$

4.2 Discretization

For the discretization of the domain $\Omega = [0, 1]^d \in \mathbb{R}^d$ we define a grid

$$\mathcal{G}_h^d := \left\{ (x_{1,i_1}, x_{2,i_2}, \ldots, x_{d,i_d}) |\ x_{l,i_j} = i_j \cdot h_l,\ i_j = 0, \ldots, n_l - 1\ j, l = 1, \ldots, d \right\},$$

with $h_l = 1/(n_l - 1)$. Then the inner points of the discrete domain are

$$\Omega_h^d = \left\{ (x_{1,i_1}, x_{2,i_2}, \ldots, x_{d,i_d}) |\ 1 \leq i_j \leq n_j - 2,\ j = 1, \ldots, d \right\},$$

and the set of discrete boundary points is defined by

$$\partial \Omega_h^d := \Gamma_h^d = \left\{ (x_{1,i_1}, x_{2,i_2}, \ldots, x_{d,i_d}) |\ \exists j : i_j \in \{0, n_j - 1\} \right\}.$$

We can also write

$$\begin{aligned} \Omega_h^d &= \mathcal{G}_h^d \cap \Omega^d, \\ \partial \Omega_h^d &= \Gamma_h^d = \mathcal{G}_h^d \cap \Gamma^d. \end{aligned}$$

For G_k we have

$$\begin{aligned} G_{h,k}^d &:= \Omega_h^d \cap (G_k \cup \mathcal{U}(G_k)), \\ \Omega_h'^d &:= \Omega_h^d \setminus G_{h,k}^d, \end{aligned}$$

where $\mathcal{U}$ is a set of points in the neighborhood of G_k which depends on the discrete approximation of external force $f(u(x))$. Specifically $\mathcal{U}(G_k)$ has to be chosen such that there exists no $x = (x_{1,i_1}, \ldots, x_{d,i_d})$ used in the discrete approximation of $f(u(x))$ that is in $\Omega_h^d \cap G_k$.

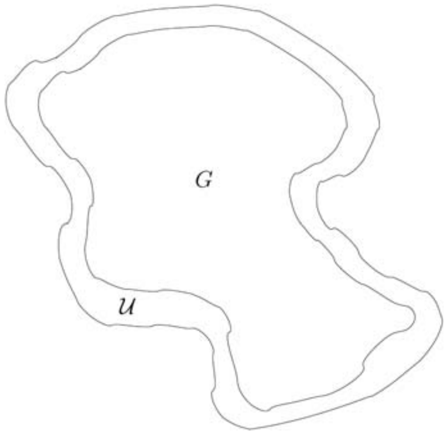

Fig. 1. Depending on the approximation G_k has to be enlarged by $\mathcal{U}$ to avoid that points in G_k are used in the approximation of f.

Example 1. When only the direct neighbors are involved in the discrete approximation of $f(u(x))$, then we have

$$\mathcal{U} := \{x|\ x \pm e_j \cdot h \in G,\ x \in \Omega',\ 1 \leq j \leq d\}.$$

We shall see that this is exactly the case for the approximation that is introduced in the following sections.

For $x \in \bar{\Omega}_h^d$ and $u(x)$ we define the following alternative notation :

$$(x_{1,i_1}, x_{2,i_2}, \ldots, x_{d,i_d})^t \mathrel{\hat{=}} x_{i_1 i_2 \ldots i_d},$$
$$u(x_{i_1 i_2 \ldots i_d}) \mathrel{\hat{=}} u_{i_1 i_2 \ldots i_d}.$$

4.3 Approximation

From (12) and (13) we obtain the system of partial differential equations

$$-\mu \left(\sum_{j=1}^{d} \frac{\partial^2 u_i}{\partial x_j^2} \right) - (\lambda + \mu) \frac{\partial}{\partial x_i} \left(\sum_{j=1}^{d} \frac{\partial u_j}{\partial x_j} \right) = f_i(u), \quad i = 1, \ldots, d, \tag{14}$$

where

$$f_i(u) = \begin{cases} (T(x - u(x)) - R(x)) \frac{\partial}{\partial x_i} T(x - u(x)) & \text{, for } x \in \Omega_h^{\prime d} \\ 0 & \text{, otherwise} \end{cases}. \tag{15}$$

Higher order terms of the Jacobian $J(x - u(x))$ have been omitted, i.e. $J(x - u(x))$ has been replaced by the identity. The partial derivatives are approximated using the finite differences approximations