Computational Methods in Biomedical Imaging

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INTRODUCTION

Biomedical imaging represents a practical and conceptual revolution in the applied sciences of the last thirty years. Two basic ingredients permitted such a breakthrough: the technological development of hardware for the collection of detailed information on the organ under investigation in a less and less invasive fashion; the formulation and application of sophisticated mathematical tools for signal processing within a methodological setting of truly interdisciplinary flavor.

A typical acquisition procedure in biomedical imaging requires the probing of the biological tissue by means of some emitted, reflected or transmitted radiation. Then a mathematical model describing the image formation process is introduced and computational methods for the numerical solution of the model equations are formulated. Finally, methods based on or inspired by Artificial Intelligence (AI) frameworks like machine learning are applied to the reconstructed images in order to extract clinically helpful information.

Important issues in this research activity are the intrinsic numerical instability of the reconstruction problem, the convergence properties and the computational complexity of the image processing algorithms. Such issues will be discussed in the following with the help of several examples of notable significance in the biomedical practice.

BACKGROUND

The first breakthrough in the theory and practice of recent biomedical imaging is represented by X-ray Computerized **Tomography** (CT) (Hounsfield, 1973). On October 11 1979 Allan Cormack and Godfrey Hounsfield gained the Nobel Prize in medicine for the development of computer assisted tomography. In the press release motivating the award, the Nobel Assembly of the Karolinska Institut wrote that in this revolutionary diagnostic tool "the signals[...]are stored and mathematically analyzed in a computer. The computer is programmed to reconstruct an image of the examined cross-section by solving a large number of equations including a corresponding number of unknowns". Starting from this crucial milestone, biomedical imaging has represented a lively melting pot of clinical practice, experimental physics, computer science and applied mathematics, providing mankind of numerous non-invasive and effective instruments for early detection of diseases, and scientist of a prolific and exciting area for research activity.

The main imaging modalities in biomedicine can be grouped into two families according to the kind of information content they provide.

- **Structural imaging**: the image provides information on the anatomical features of the tissue without investigating the organic metabolism. Structural modalities are typically characterized by a notable spatial resolution but are ineffective in reconstructing the dynamical evolution of the imaging parameters. Further to X-ray CT, other examples of such approach are Fluorescence Microscopy (Rost & Oldfield, 2000), Ultrasound Tomography (Greenleaf, Gisvold & Bahn, 1982), structural Magnetic Resonance Imaging (MRI) (Haacke, Brown, Venkatesan & Thompson, 1999) and some kinds of prototypal non-linear tomographies like Microwave Tomography (Boulyshev, Souvorov, Semenov, Posukh & Sizov, 2004), Diffraction Tomography (Guo & Devaney, 2005), Electrical Impedance Tomography (Cheney, Isaacson & Newell, 1999) and Optical Tomography (Arridge, 1999).
- **Functional imaging**: during the acquisition many different sets of signals are recorded according to a precisely established temporal paradigm. The resulting images can provide information on metabolic deficiencies and functional diseases

but are typically characterized by a spatial resolution which is lower (sometimes much lower) than the one of anatomical imaging. Emission tomographies like Single Photon Emission Computerized Tomography (SPECT) (Duncan, 1997) or Positron Emission Tomography (PET) (Valk, Bailey, Townsend & Maisey, 2004) and Magnetic Resonance Imaging in its functional setup (fMRI) (Huettel, Song & McCarthy, 2004) are examples of these dynamical techniques together with Electro- and Magnetoencephalography (EEG and MEG) (Zschocke & Speckmann, 1993; Hamalainen, Hari, Ilmoniemi, Knuutila & Lounasmaa, 1993), which reproduce the neural activity at a millisecond time scale and in a completely non-invasive fashion.

In all these imaging modalities the correct mathematical modeling of the imaging problem, the formulation of computational algorithms for the solution of the model equations and the application of image processing algorithms for data interpretation are the crucial steps which allow the exploitness of the visual information from the measured raw data.

MAIN FOCUS

From a mathematical viewpoint the **inverse problem** of synthesizing the biological information in a visual form from the collected radiation is characterized by a peculiar pathology.

The concept of **ill-posedness** has been introduced by Jules Hadamard (Hadamard, 1923) to indicate mathematical problems whose solution does not exist for all data, or is not unique or does not depend uniquely on the data. In biomedical imaging this last feature has particularly deleterious consequences: indeed, the presence of measurement noise in the raw data may produce notable numerical instabilities in the reconstruction when naive approaches are applied.

Most (if not all) biomedical imaging problems are ill-posed inverse problems (Bertero & Boccacci, 1998) whose solution is a difficult mathematical task and often requires a notable computational effort. The first step toward the solution is represented by an accurate modeling of the mathematical relation between the biological organ to be imaged and the data provided by the imaging device. Under the most general assumptions the model equation is a non-linear integral equation, although, for several devices, the non-linear imaging equation can be reliably approximated by a linear model where the integral kernel encodes the impulse response of the instrument. Such linearization can be either performed through a precise technological realization, like in MRI, where acquisition is designed in such a way that the data are just the Fourier Transform of the object to be imaged; or obtained mathematically, by applying a sort of perturbation theory to the non-linear equation, like in diffraction tomography whose model comes from the linearization of the scattering equation.

The second step toward image reconstruction is given by the formulation of computational methods for the reduction of the model equation. In the case of linear ill-posed inverse problems, a well-established **regularization** theory exists which attenuates the numerical instability related to ill-posedness maintaining the biological reliability of the reconstructed image. Regularization theory is at the basis of most linear imaging modalities and regularization methods can be formulated in both a probabilistic and a deterministic setting. Unfortunately an analogously well-established theory does not exist in the case of non-linear imaging problems which therefore are often addressed by means of 'ad hoc' techniques.

Once an image has been reconstructed from the data, a third step has to be considered, i.e. the processing of the reconstructed images for the extraction and interpretation of their information content. Three different problems are typically addressed at this stage:

- **Edge detection** (Trucco & Verri, 1998)**.** Computer vision techniques are applied in order to enhance the regions of the image where the luminous intensity changes sharply.
- **Image integration** (Maintz & Viergever, 1998). In the clinical workflow several images of a patient are taken with different modalities and geometries. These images can be fused in an integrated model by recovering changes in their geometry.
- **Image segmentation** (Acton & Ray, 2007). Partial volume effects make the interfaces between the different tissues extremely fuzzy, thus complicating the clinical interpretation of the restored images. An automatic procedure for the partitioning of the image in homogeneous pixel sets and for

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