Biomechanical functional and sensory modelling of the gastrointestinal tract

BY DONGHUA LIAO1,*, DINA LELIC1,2, FENG GAO1, ASBJØRN MOHR DREWES1,2 AND HANS GREGERSEN1,2,3

1Mech-Sense, Aalborg Hospital Science and Innovation Centre, Søndre Skovvej 15, 9000 Aalborg, Denmark
2Institute of Health Technology, Aalborg University, 9100 Aalborg, Denmark
3National Center of Ultrasound in Gastroenterology, Bergen University and Haukeland Hospital, 5021 Bergen, Norway

The aim of this review is to describe the biomechanical, functional and sensory modelling work that can be used to integrate the physiological, anatomical and medical knowledge of the gastrointestinal (GI) system. The computational modelling in the GI tract was designed, implemented and evaluated using a series of information and communication technologies-based tools. These tools modelled the morphometry, biomechanics, functions and sensory aspects of the human GI tract. The research presented in this review is based on the virtual physiological human concept that pursues a holistic approach to representation of the human body. Such computational modelling combines imaging data, GI physiology, the gut–brain axis, geometrical and biomechanical reconstruction, and computer graphics for mechanical, electronic and pain analysis. The developed modelling will aid research and ensure that medical professionals benefit through the provision of relevant and precise information about a patient’s condition. It will also improve the accuracy and efficiency of the medical procedures that could result in reduced cost for diagnosis and treatment.

Keywords: gastrointestinal tract; computational modelling; biomechanics; function; sensory

1. Introduction

Computer-based analysis, visualization, modelling and simulation are used routinely in engineering and other fields to understand the behaviour and outcomes of new designs and the impact of external phenomena well before their realization, thereby avoiding costly failures. In the healthcare sector, this approach is not common but is evolving (Hunter et al. 2002; Hunter & Nielsen 2005; * Author for correspondence (dliao@hst.aau.dk).

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Clapworthy & Viceconti 2007). Exploration of the human body has dramatically improved by the introduction of medical imaging modalities such as magnetic resonance imaging (MRI) and ultrasonography (Frokjaer et al. 2005, 2006; Gilja et al. 2007). These techniques have revolutionized the way in which many conditions are diagnosed and treated. The ability to examine in detail structures inside the body, without surgery access, has allowed clinicians to diagnose disease at an early stage (Berstad et al. 1996, 1998; Gilja et al. 2006). This allows the planning of interventional procedures with a minimum risk to the patient. In order to continue this exploration, it will be necessary to complement the traditional approach with an integrative approach. This will combine observations, theories and predictions across the temporal and dimensional scales, the scientific disciplines and the anatomical subsystems, all of which reflect the rather artificial divisions described.

A mix of policy and research activities promoting a shift from population- to person-centred systems and from reactive to proactive (preventive) healthcare is part of a broader strategic approach of the European Commission in the eHealth domain. Within this environment, it is widely envisaged that modelling and simulation can be adopted by the healthcare industry to understand the complexity of human physiology and predict human response to therapies (Hunter et al. 2002; Hunter & Nielsen 2005; Clapworthy & Viceconti 2007). Additionally, virtual human organs may be used to understand the impact of patient variability on these predictions. This topic of modelling and simulation of the human physiology for better understanding and cure of diseases has recently received great attention from the academic, clinical and commercial communities (Hunter et al. 2002; Hunter & Nielsen 2005; Clapworthy & Viceconti 2007).

The aim of this review is to describe the currently developed biomechanical, functional and sensory modelling work in the gastrointestinal (GI) tract that can be further used to integrate the physiological, anatomical and medical knowledge of the GI system.

2. Anatomy and function of the GI tract

The GI tract, also called the digestive tract or the alimentary canal, is the system of organs within multicellular animals that takes in food, digests it to extract energy and nutrients and expels the remaining waste. The GI tract is a continuous channel through the body with the biliary and pancreatic ducts as major side branches. The main functions of the GI tract are transport and digestion of food. However, the gut is also important for immune functions (Gregersen 2002). The GI tract consists of a series of organs that resemble one another in constitution, being variously arranged as cylinders, spheroids or intermediate forms. The wall of the GI tract is a laminated composite structure (figure 1). The general structure is an outer muscle coat consisting of an outer longitudinal and an inner circular muscle layer. The collagen-rich submucosa and mucosa layers are found inside the outer muscle coat. A third layer of muscle, the muscularis mucosae, exists throughout almost the entire tract. The motions of the GI tract must, at all times, accomplish a net antegrade flow in order to mix the contents and move it across the surface where absorption occurs. The contractile patterns and transit vary greatly from one part of the tract to another. A network of nerves, the
myenteric plexus, is embedded in the loose collagen matrix between the longitudinal and circular muscle layers. This set of nerves is essential in the regulation of the contractions of the adjacent musculature. Between the nerve endings and smooth muscle are contained the interstitial cells of Cajal (ICCs), a special set of modified muscle cells. ICCs have been recognized as important elements in the regulation of GI motility. Specifically, they have been shown to be critical for the generation and propagation of electrical slow waves that regulate the phasic contractile activity of GI smooth muscle, and for mediating neurotransmission from enteric motor neurons to smooth muscle cells (Sanders et al. 2002; Burns 2007). The enteric nervous system (ENS), composed of both the myenteric (inter-muscular) plexus and the submucosal plexus, is also distributed in the GI tract from the oesophagus to the internal anal sphincter (Takaki 2003). The ENS contains approximately 100 million neurons, which is the largest accumulation of nerve cells outside the brain. It has structural and functional similarities to the brain and can be considered an autonomic nervous system of the gut. The ENS ensures that the GI tract can fulfil essential tasks even when isolated from the rest of the body. The GI tract is, on the other hand, unable to work normally without the integrative functions of the ENS. Accordingly, malfunctions of integrative ENS control of the digestive effector systems are increasingly recognized as underlying factors in many GI diseases. The exogenous nerves running together with the sympathetic and parasympathetic nervous systems are also important in the normal regulatory functions, related to blood flow, secretion, etc. (Guyton & Hall 2000). They also encode the conscious sensations from the gut such as fullness, urge to defecation and, under pathological circumstances, pain (Drewes et al. 2003). The various patterns of GI tract function are generated by the integrated behaviour of multiple tissues and cell types. Medical imaging methods such as ultrasonography, MRI and endoscopic ultrasound are well-known stand-alone clinical methods that can disclose structural and functional abnormalities of the GI tract (Camilleri 2006; Gilja et al. 2007). As the GI tract basically acts as a mechanical system, biomechanical and bioengineering principles can be applied to most problems related to the function and pathophysiology.
3. Biomechanical modelling of the GI tract

Gastroenterology research has traditionally been based on experimental approaches rather than on mathematical modelling. However, in the past 5–10 years, several groups have independently started to model the GI tract and accordingly Gregersen introduced the term ‘GIOME’ in 2003 (Gregersen 2006). Thus, the Physiome-based GIOME project is a new concept in gastroenterology. Multiscale mathematical and computer models are developed within this concept in order to understand human health. From its beginning, approximately 15 years ago, most Physiome effort has been in the cardiac and lung field (the Cardiome project; Hunter et al. 1992, 2002; Smith et al. 2000, 2002; McCulloch & Huber 2002; McCulloch 2004; Hunter & Nielsen 2005), but other areas are now established as development research fields. The modelling work in the GI tract so far has been on the mechanics and electromechanical properties at the tissue and organ level based on medical imaging and other advanced techniques (Drewes et al. 2003; Drewes & Gregersen 2006). The relationship among the mechanical behaviour, modelling geometry features and sensory aspects has been simulated in several GI organs. Our methods for generating GI tract biomechanical models are briefly introduced below on the basis of the developed mechanical tests, geometric, surface, finite-element models and functional models.

(a) Mechanical properties of the GI tissues

The effectiveness of using the numerical modelling analysis depends on reliable reconstructions of the morphometry of the anatomical site under investigation and the specific loading and boundary conditions, as well as on the definition of constitutive models capable of describing the mechanical response of a single tissue (Natalia et al. 2006a,b). The most current investigations of the GI tissue properties are mainly focused on seeking the constitutive equation and the associated constitutive parameters of the physiological or pathological status (Gregersen 2002; Liao et al. 2003; Zhao et al. 2003, 2007; Yang et al. 2004, 2006; Lu et al. 2005). Most GI structure and tissue property studies have been based on animal experiments so far. Medical device development has made it possible to study the mechanical behaviour of the GI tract in vivo (Drewes et al. 2003, 2006; Pedersen et al. 2005; Gregersen et al. 2006, 2007; Frokajaer et al. 2006). However, the GI tract tissue consists of four different layers with different fibre directions. Previous modelling and experimental studies on the multi-layered oesophagus indicated that the GI tract must be simulated as multi-layered composite structures during modelling analysis (Liao et al. 2003, 2004b; Yang et al. 2007a). By using the advanced ultrasonographic technology, it is now possible to distinguish the layered structures of the GI organs in vivo (Nicosia et al. 2001; Gasser et al. 2006; Brasseur et al. 2007). Furthermore, the multimodal probe developed by our group can record the luminal pressure and luminal cross-sectional area (CSA) simultaneously on several GI organs. Hence, the tissue properties of the different layers of the GI organs are now possible to obtain in vivo by combining the multimodal probe recorder and the ultrasonographic images (Frokajaer et al. 2006a,b).
The anisotropic feature of the GI organs has been included in most of the constitutive equations of the GI tract (Gregersen 2002; Liao et al. 2003; Yang et al. 2006a,b, 2007c). However, the muscle and collagen fibre effects on the constitutive equations were neglected in most of the GI tissue property studies. Several fibre orientation-based constitutive equations have been developed in biomechanical studies on the cardiovascular system and are now introduced in oesophageal modelling analysis (Holzapfel et al. 2004; Gasser et al. 2006; Yang et al. 2007c). The fibre structure of the GI organs is now possible to be quantified by using diffusion spectrum MR imaging (Gilbert et al. 2006a,b). Hence, the fibre structure should be taken into account in further GI organ property research.

(b) Geometric modelling

The geometric modelling is the fundamental part of the GI modelling analysis. Owing to the complex geometry of the GI organs, three-dimensional models of the GI tract are considerably important. Advances in imaging are being introduced initially as research tools and subsequently as clinical diagnostic tests. Medical imaging-based three-dimensional models of in vivo GI organs have characterized the oesophagus, stomach, small intestine, sigmoid colon and rectum using ultrasonography, computed tomography (CT) or MRI (Li et al. 1994; Liao et al. 2004a; Frokjaer et al. 2005, 2007; Jeays et al. 2007a,b; Pal et al. 2007). Figure 2 shows an example of reconstruction of the stomach shape obtained by three-dimensional ultrasonography. The main methods we used for the three-dimensional GI geometric modelling establishment are briefly described below. More detailed description of the methods can be found in our previous literature in Liao et al. (2004a, 2005) and Frokjaer et al. (2005, 2007).
Medical imaging-based three-dimensional model reconstruction

The initial three-dimensional GI models were reconstructed on the basis of images from ultrasonography, CT or MRI. With the identified inner and outer wall boundaries of each cross-sectional two-dimensional image, a data cloud of a three-dimensional model was then obtained by using a segmentation technique. For GI organs, such as the stomach (Liao et al. 2004a), rectum (Frokjaer et al. 2005) or sigmoid colon (Frokjaer et al. 2007; figure 3), the centre line of the organs is curved. When the organ is deformed, it is deformed along the curved axis. Therefore, alignment of data points along this curved centre line was necessary to describe the GI model deformation. Based on a three-dimensional solid model generated from the cross-sectional images, it can be re-sliced along the curved centre line and the surface model based on the re-sliced images can be obtained. Figure 3 shows a sigmoid colon solid model and a surface model generated from the re-sliced images.

Figure 3. (a) A sigmoid colon solid model generated directly on the basis of the three-dimensional data cloud and (b) a smoothed surface model generated from the pictures re-sliced along the centre line of the solid model. The black lines in (a) are the slices along the centre line of the solid model.

(i) Medical imaging-based three-dimensional model reconstruction

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(ii) Surface smoothing

The reconstructed surfaces have some irregularities due to the discretization of the images. The irregularities were removed using two different smoothing methods described in our previous studies. One method is based on the Fourier transform algorithm and another one is a modified non-shrinking Gaussian smoothing method. For detailed description of these two smoothing algorithms, the reader is referred to our previous papers (Liao et al. 2004a, 2005). Based on the continuous and smoothed surface, the surface can be approximated locally by a biquadric surface patch. The parametric surface used in our studies is a tensor product B-spline surface, which gives the necessary continuity properties with good surface approximation (Dierckx 1993).

The smoothed surface was validated by comparing with the solid model reconstructed directly from the medical images for a good correction.

(iii) Curvature calculation

On the basis of the smoothed parametric surface, the surface geometric features, such as principal curvatures of the surface \(k_1\) and \(k_2\), can be generated from the coefficient of the first fundamental form \((E, F, G)\) and the second fundamental form \((L, M, N)\) of the parametric surface function. Figure 4a shows the circumferential curvatures’ distribution on a human rectum model.

(c) Thin-wall surface modelling of the GI tract

With the obtained curvatures’ distribution of the surface modelling, assuming that the GI organs are thin walled and the material properties are isotropic, the surface tension \(T\) at a surface point is related to the transmural pressure by Laplace’s equation as follows:

\[ p = T[k_1 + k_2], \]

(3.1)

where \(k_1\) and \(k_2\) are the principal surface curvatures at a surface point. This equation is valid as long as the membrane is so thin that bending rigidity can be neglected and the curvature changes are not sudden. Accordingly, only the spatial points with both positive curvatures were used for tension (and stress) calculations in this study.

Stress is defined as the force acting on a unit area. The stress distribution on the surface can be calculated from wall tension and normal wall thickness as

\[ \sigma = \frac{T}{h}, \]

(3.2)

where \(T\) is the surface tension and \(h\) is the normal wall thickness. Examples of tension and stress distribution on the rectum model are illustrated in figure 4b,c.

The three-dimensional model reconstruction and the tension, stress calculations described above were only based on the medical images, omitting the information about the tissue material properties and the tissue structures. Therefore, the methods described in this section can be further extended clinically for an individual patient-based computational GI tract model analysis.

(d) Finite-element modelling of the GI tract

The large morphological complexity of the GI tract and the variability in the different GI organs are well known. The complexity increases in the layered composite structure and the varied fibre orientations in each layer.
As a consequence, the GI tract tissue must be considered as multi-layered with fibre-reinforced composite material. Therefore, Laplace’s equations for tension and stress calculations (figure 4b, c) were limited in the thin-wall assumption and only the surfaces with positive principal curvatures in both longitudinal and circumferential directions were valid for the calculation. To overcome this limitation, numerical methods such as finite-element analysis must be adopted since the finite-element analysis potentially offers high structural hierarchy and constituents with nonlinear behaviour in the analysis of the mechanical behaviour. The morphological complexity of the GI organs makes it difficult to build anatomy-based finite-element models. Hence, some numerical models of the GI organs were simplified as a regular geometry such as a circular cylinder for the oesophagus (Li et al. 1994; Yang et al. 2007a, b) and sphere for the stomach pouch (Gao et al. 2008). However, with the development of the medical image technology and the Physiome project, more and more anatomy-based GI models have been established, such as the finite-element models used for modelling GI tract bioelectric activity (Buist et al. 2004, 2006; Pullan et al. 2004; Yassi et al. 2004; Lin et al. 2006a, b; Cheng et al. 2007), the layered oesophageal model (Liao et al. 2004a, b) and stomach emptying model (Pal et al. 2007).

Figure 4. (a) The circumferential curvature, (b) the tension and (c) the stress distributions on a rectum model with distension volume of 200 ml. The empty area (white area) in (b, c) means the surface point with a negative longitudinal curvature that means a sudden change of the surface curvatures and therefore Laplace’s law was not valid for the tension and stress calculation.
Figure 5. (a) The three-dimensional pouch finite-element model, (b) stress and (c) strain distributions in a pouch model before emptying.

(e) Functional modelling

To achieve the function of the GI tract, it requires the coordinates of food movement, secretion, absorption, circulation and nerve control. It is well known that the biomechanical behaviour of the GI tract is function related. The GI tract acts as a mechanical system and performs primarily mechanical functions, therefore biomechanical and bioengineering principles can be applied to almost any problem related to GI function and pathophysiology. Previous studies of biomechanical behaviour of the GI organs were mainly based on extensive experimental activity. With the capability of improved computational methods and experimental measurement, numerical analysis can be exploited to better understand the GI physical and pathophysiological functions on the basis of the biomechanical characteristics, such as the food transportation (Li et al. 1994; Pal et al. 2007; Yang et al. 2007c), the electromechanical activity (Pullan et al. 2004; Cheng et al. 2007), blood circulation (Mabotuwana et al. 2006; Jeays et al. 2007a,b) and mixing (Dillard et al. 2007). Here, two clinical problem-based examples of the functional model generated in our previous study are introduced. More information about these two examples can be found in the literature of McMahon et al. (2004, 2007) and Gao et al. (2008).

(i) In vivo three-dimensional oesophago-gastric junction profiles

A simple impedance technique has been used extensively to determine the luminal CSA in the hollow organs of the body and, in particular, in the GI organs (Drewes et al. 2002, 2003; Drewes & Gregersen 2006). Impedance

Phil. Trans. R. Soc. A (2008)
planimetry was recently further developed into multi-electrode systems for the purpose of measuring a number of cross sections inside a saline-filled bag (Andersen et al. 2004) and in the oesophago-gastric junction (OGJ; McMahon et al. 2004); that is, a functional lumen imaging probe (FLIP) to measure eight CSAs has been developed. FLIP is a new technique to provide serial luminal images of the functioning digestive tract using multiple electrical impedance recordings within a bag placed in the GI lumen. From such measurements, geometric profiles of the organ can be modelled in real time (functional animations). The eight CSAs measured by FLIP gave a unique way to describe the three-dimensional outline of the geometric profile of the sphincter at various levels of balloon distension in vivo (McMahon et al. 2007). The accepted understanding of OGJ function is that it closes off to stop the refluxing of stomach contents into the oesophagus. This closing off must be related to a narrowing of the lumen, which can be represented by CSAs measured in this region. The in vivo three-dimensional outlines of the OGJ could represent a major step forward in the diagnosis, monitoring and evaluation of diseases such as GERD and achalasia.

(ii) Filling and emptying simulation of the small stomach made in laparoscopic adjustable gastric banding surgery

Gastric accommodation and gastric emptying are two major functions of the stomach. Owing to the complex stomach geometry and tissue structures, it is difficult to simulate the whole gastric function numerically. Gastric emptying in a two-dimensional gastric model has been simulated recently (Pal et al. 2007). However, only the flow feature in the gastric lumen was simulated in such two-dimensional models and the gastric wall mechanical behaviour was neglected. Recently, we have developed a simplified gastric model specific for simulating the filling and emptying phases of a gastric pouch produced in laparoscopic adjustable gastric banding surgery (figure 5; Gao et al. 2008). Several studies have indicated that the pouch volume and the stoma size are the two important factors related to the weight loss (Forsell 1996; Roberts et al. 2007). However, more quantitative data are needed to learn more about the mechanism for the induced weight loss. Nevertheless, no study has thoroughly investigated the effect of pouch size or stoma diameter using otherwise identical operations. The great variety of the restrictive procedures and of the pouch makes comparison impossible. Modelling and numerical simulation can provide qualitatively reliable investigation for the effects of pouch volume and stoma diameter on the stress and strain. Hence, we established the pouch model with various pouch volumes and stoma sizes in order to see whether the association between the degree of filling of the pouch, the stress and strain of the pouch wall, and the feeling of satiety and weight loss exists. The numerical simulation indicated that the simulated pouch emptying curve fits well with the clinical recorded curves and both pouch volume and stoma size were important determinants for mechanical wall stress. This provides a feasible explanation for the reduced weight loss in patients with large pouches, assuming that wall stress and strain determine the symptom pattern during eating.

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4. Integrated mechanical sensory modelling

Existing investigations of GI biomechanical analysis are mainly focused on passive mechanical behaviour of the GI tract and the neuron-controlled muscle active behaviour is neglected. For understanding the principle of the smooth muscle activity, the interaction among the muscle, motor neurons of the ENS and the ICCs should be described on the basis of the electromechanical and pharmacomechanical coupling from the ionic to cell to tissue level. Bornstein and colleagues are developing models of ENS and have done a number of studies on mice and guinea-pigs, which suggest that their models can make reliable representations of enteric neural circuitry across different species (Bornstein et al. 2002; Bornstein 2006). Vagal and spinal afferent fibres terminate within the muscle layers of the GI tract, and most vagal afferent fibre endings to the muscle layer of the gut comprise two specialized endings, intraganglionic laminar endings (IGLEs) and intramuscular arrays. IGLEs have long been speculated to function as mechanoreceptors within the gut (Beyak et al. 2006). Different forms of mechanical stimulation have been used to investigate the neurophysiologic properties of mechanoreceptors of the GI tract. The balloon distension causing afferent fibre activities indicated that the afferent spike rate is associated with the tension and deformation activated on the tissue (Daly et al. 2007). Mathematical modelling may be used to explore those consequences by systematically including or excluding each neuronal feature from the model and carrying out computational experiment. The single cell neuron model in the GI tract for describing the interaction between the excitation–contraction coupling on the molecular and cell level has been developed theoretically on the adrenergic neuron and cholinergic neuron (Miftakhov & Wingate 1994a,b), and the stretch-activated action has now been added into a cardiac cells model (Healy & McCulloch 2005). Moreover, an experimental method is now available to detect the neuron distribution on one IGLS and to track single neuron activity in one single IGLS (Schemann et al. 2002; Blackshaw et al. 2007). Therefore, we believe that the ENS research has now reached a stage at which theoretical thinking and mathematical modelling have become essential to integrate and make sense of the biological information being generated and, more importantly, to generate new biological hypotheses that can then be tested in the laboratory.

The study of pain has become a multidisciplinary enterprise in the search for greater understanding of this puzzling and multifaceted phenomenon (Britton & Skevington 1996). Different forms of mechanical stimulations have been used to investigate the neurophysiologic properties of mechanoreceptors of the GI tract. The amount of experimental data on visceral pain that is now available is so enormous that it is becoming increasingly difficult to see the forest for the trees, and a simple theory of the functional consequences of any particular neuronal feature may not be apparent. Pain messages are two-way traffic: (i) the ascending pathways that convey information from peripheral nociceptors to higher levels of the central nervous system and (ii) the descending feedback pathways that inhibit or facilitate pain intensity. Experimental data on visceral pain are now available for both the ascending and descending pathways. Although experimental analysis is a precondition for understanding visceral pain, it is by no means sufficient. The understanding is aided at all levels of complexity by signal analysis and modelling.
5. Modelling brain activity to GI pain

(a) Brain imaging

As pain is a conscious feeling, the ultimate goal is to follow the pain stimulus throughout the neuraxis. Human studies based on positron emission tomography (PET) and functional MRI (fMRI) in healthy subjects have shed light over the brain processing of pain. PET can measure the cerebral blood flow after injection of a radioisotope, whereas MRI is based on the different paramagnetic properties of oxy- and deoxyhaemoglobin in the blood. Both PET and fMRI have excellent spatial resolution (2–5 mm) but relatively poor temporal resolution (minutes for PET and several seconds for fMRI)—as it takes some time for changes in blood flow to occur. Thus, these methods do not image the neuronal activity directly but demonstrate changes in blood flow in the regions activated (or deactivated) during pain stimuli. The brain’s response to exogenous stimulations takes place within 100–150 ms after the stimulations. Therefore, the responses recorded in fMRI and PET can be non-specifically related to arousal, attention, emotions and other secondary (endogeneous) processing rather than pain. By contrast, cortical evoked potentials (CEPs) detect the neuronal activity in real time, with a temporal resolution on the millisecond scale. When repetitive stimuli are applied and the cortical electrical activity is averaged, the evoked potentials can be extracted from the background electrical activity and they are shown in the shape of a waveform with different peaks. Each peak in the CEP represents a synaptic event associated with the transmission of afferent information from one group of neurons to another. Figure 6a shows the typical topography of CEPs corresponding with the early pain-specific brain activation to stimulation of the colon. Reduction in latency of the evoked brain potentials may be related to hyperexcitability within central pain pathways evoked by chronic pain attacks in patients. This is most probably caused by opening of latent faster conducting connections. Several studies have examined evoked brain potentials in various diseases, but studies in larger patient groups where external factors are controlled, are highly warranted.

(b) Inverse modelling of the electrical brain activity to experimental pain

The study of CEPs has limitations with a low spatial resolution due to distortion of the signal and overlapping of neuronal activities. However, methods using advanced signal analysis can be used to address such problems. By recording CEPs from multiple sites on the scalp simultaneously, it is possible to calculate the cerebral sources generating the electromagnetic fields. This is called ‘inverse modelling’. In short, electrical activity in assemblies of neurons (such as cellular columns) can be modelled by an equivalent dipole, being a linear source (e.g. battery) with two opposing poles. These dipoles play a major role in the generation of the electrical and magnetic fields at the skull surface. Each dipole represents the sequential activation/deactivation of the brain to synchronized peripheral pain stimuli. The dipoles can be projected onto the Talairach and Tournoux stereotactic brain atlas or the MRI of the subject’s brain, and their anatomical position can be estimated (figure 6b).

Several algorithms have been proposed and implemented in order to determine the active brain sources, given the surface EEG signal alone. Inverse modelling algorithms have usually been applied to instantaneous data using commercially
available methods such as low-resolution brain electromagnetic tomography (LORETA) and multiple signal classification. However, disadvantages of doing inverse modelling this way are the instability of algorithms when modelling multiple sources and the interference of background noise. For this reason, space–time-based signal decompositions have been used prior to inverse modelling, such as independent component analysis and blind source separation (Makeig et al. 1996; Belouchrani et al. 1997; Drewes et al. 2006), but these algorithms are based on some strong assumptions about the data among which are linearity and some statistical independence of the sources. Recently, multichannel matching pursuit
(MMP) has been used as a decomposition method where the EEG data are decomposed into a sum of waveforms, usually termed atoms, each being defined in time, frequency and space (Durka et al. 2005). Furthermore, MMP does not make strong assumptions about the independence of generators’ activities. Once the data are decomposed, inverse modelling is performed on each of the atoms (figure 6b). In a preliminary study where we simulated CEP data with known dipole locations, we compared application of inverse modelling directly to these data and decomposed data using several different decomposition methods, including MMP (D. Lelic et al. 2008, unpublished data). We observed that MMP localized cortical and deep sources with much higher accuracy than other methods. This was later reproduced in human experiments where the median nerve somatosensory evoked potentials and flashlight visual evoked potentials were examined. Hence, MMP allows us to observe time and frequency activation of cortical and deep brain centres when provided with only the EEG data, and can be used in CEP studies where pain is experimentally applied in order to study the brain centre activation sequence due to pain.

(c) Cortical reorganization

Several experimental and clinical studies have indicated that deafferentation, chronic pain and hyperalgesia are associated with functional reorganization of the cortex. In particular, there is evidence for neuroplastic changes and reorganization of the brain in patients with amputations and neuropathic pain. Importantly, the amount of cortical reorganization correlates with the subjective pain rating, and the cortical changes can be reversed by analgesic interventions. Diseases of the gut thought to have a strong neurogenic component such as chronic pancreatitis also show evidence for cortical reorganization. In recent experiments done by our group, analysis of the brain sources to upper gut stimulations showed that the insular activity was reorganized in pancreatitis patients with pain (Dimcevski et al. 2007). There were also more discrete changes in the cingulate gyrus where the neuronal source was more posterior in patients. The findings indicate that pain in chronic pancreatitis leads to changes in cortical projections of the nociceptive system supporting a neuropathic component in pancreatic pain. Obviously, such cortical reorganization could also be studied in patients with other organic and functional GI disorders.

6. Perspectives

Computerized systems help analyse digital images for typical appearances and highlight conspicuous sections (possible diseases). Automated GI tract disease detection is a developing interdisciplinary technology combining elements of machine learning and digital image processing. However, the introduction of such predictive models as a means of supporting the clinical decision is in general difficult due to problems relating to building up sufficiently large databases. Such databases can contain reference cases for training and testing, developing classifiers, and ongoing developments in clinical knowledge, necessitating adjustments in the algorithms. Other factors that affect the performance of predictive models are the quality of the images employed, the condition of the examination, the investigator’s experience and education, type of pathology and its maturity.
An evolving trend towards personalized healthcare is emerging, based on the use of simulation to predict the outcome of interventions on the individual. The challenge is to develop mathematical and computational models of structure-function relations appropriate to each (limited) spatial and temporal domain and then to link the parameters of a model at one scale to a more detailed description of structure and function on the adjacent levels. Two-dimensional cross-sectional imaging (CT, MRI and ultrasonography)-based modelling has been used to characterize biomechanics, function and sensory responses in the stomach (Liao et al. 2004b, 2005), the rectum and sigmoid colon (Frokjaer et al. 2005, 2007), cardiovascular system and computer-aided orthopaedic surgery. The present analytical tool can thus be integrated in order to analyse complex structures for understanding biomechanical properties and visceral perception in other visceral organs and further to be integrated as a global GI model. The geometry and sensory aspects of diseases in the sigmoid colon (diverticular disease, irritable bowel syndrome, etc.), small bowel (motility disorders), stomach (motility disorders, non-ulcer dyspepsia, etc.) and oesophagus (oesophagitis, gastro-oesophageal reflux disease, non-cardiac chest pain, etc.) can be further developed by applying modified versions of the present modelling.

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