

Electrical impedance tomography spectroscopy (EITS) for human head imaging

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Abstract

Electrical impedance tomography (EIT) is a recently developed medical imaging method which has practical advantages for imaging brain function as it is inexpensive, rapid and portable. Its principal use in validated human studies to date has been to image changes in impedance at a single excitation frequency over time, but there are potential applications where it is desirable to obtain images from a single point in time, which could be achieved by imaging over multiple frequencies. We describe a novel multifrequency EIT design which provides up to 64 electrodes for imaging in the head. This was achieved by adding a multiplexer to a single channel of an existing system, the Sheffield Mark 3.5. This provides a flexible protocol for addressing up to 64 electrodes but CMRR decreases from 90 dB to 80 dB and analogue amplifier bandwidth from >1.6 MHz to 0.8 MHz. This did not significantly affect performance, as cylinders of banana, 10% of the diameter of a saline filled spherical tank, could be visualized with frequency referenced imaging. The design appears to have been an acceptable compromise between practicality and performance and will now be employed in clinical trials of multifrequency EIT in stroke, epilepsy and neonatal brain injury.

Keywords: electrical impedance tomography, multifrequency, hardware

1. Introduction

For a decade or so, our group at University College London has been developing the use of electrical impedance tomography (EIT) for imaging brain function. EIT of the brain has the

potential to provide a portable, non-ionizing imaging system which is suitable for long term monitoring in surgery planning for epilepsy (Holder *et al* 1994), diagnosis of acute stroke and evoked potential studies (Tidswell *et al* 2001). Hardware (Holder *et al* 1999, Fitzgerald *et al* 2002, Yerworth *et al* 2002) and reconstruction algorithms specifically for head imaging have been developed within the group (Gibson *et al* 1999, Bayford *et al* 2001, Liston *et al* 2002).

These have been used to image visual evoked potentials in humans (Tidswell *et al* 2001) and preliminary data have been obtained during seizures (Tidswell *et al* 2003). However, all this work has been limited to recording of changes in impedance over time at a single frequency. This was because systems were based, for practical reasons of robustness, on the Sheffield Mark 1 design (Brown and Seagar 1987), which could only record serially at a single excitation frequency of 50 kHz. This limited imaging to changes over time, but, in practice, this was satisfactory for recording impedance changes in cell swelling or blood flow which changed in the above conditions over several minutes (Holder 1992, Boone *et al* 1993, Holder *et al* 1996).

There are clinical conditions, such as stroke or head injury, where it is impractical to do time difference imaging because no reference image can be obtained from before the event. An example of this is in the use of thrombolytic therapy for acute stroke, which must be preceded by brain imaging to confirm the diagnosis and to differentiate ischaemic and haemorrhagic types. This is required within three hours of the onset of symptoms. At present x-ray computed tomography (CT) or magnetic resonance imaging (MRI) is used for this, but arranging a scan within three hours of the onset of symptoms is often not possible (Harraf *et al* 2002). EIT in the accident and emergency department would be an affordable and practical way to perform initial neuroimaging and permit rapid use of thrombolytic therapy.

Single EIT images may be produced either by reconstructing 'absolute' images of the impedance collected at a single time point and single frequency, or by a difference method in which impedance is recorded simultaneously at multiple frequencies, and images are reconstructed of the differences between them (EIT spectroscopy (EITS)), (Lu *et al* 1995). There are significant problems in absolute imaging, largely because of instrumentation errors due to stray capacitance. We have, therefore, elected to pursue the EITS approach, as instrumentation errors can be cancelled out to a considerable degree by the use of difference measurements. We term the resulting images below 'frequency referenced'. The impedance characteristics of the brain and cerebral tissues have been well characterized and display two major dispersions in the range dc to 1 MHz (Gabriel *et al* 1996a, 1996b, Duck 1990). The complex impedance of brain changes due to mechanisms such as cell swelling or infusion with blood during conditions such as stroke or spreading depression (Holder 1992, Ranck 1964), so there are good grounds for anticipating that EITS could be used clinically to image these changes.

A system has been designed specifically for head imaging in our group, the UCLH Mk1b (Yerworth *et al* 2002). Although it can record at any one of a range of frequencies between 225 Hz and 77 kHz, it is not ideal for simultaneous spectroscopic imaging, as it is designed for recording changes over time at a single selected frequency, rather than rapid sweeping through frequencies. It utilizes a single analogue impedance measuring circuit, which is multiplexed to up to 64 electrodes (figure 1). The current source is based on a current conveyer voltage to current converter (CCII01) (Toumazou *et al* 1990). Electrodes are selected using a set of cross-point switches (MITEL MT8816), which enables any combination of drive and receive electrodes to be selected. The system operates at a single frequency, selectable from 18 frequencies between 225 Hz and 77 kHz. Unscreened cables are used to reduce the weight and bulk of leads. The common mode performance of the system is enhanced by isolating

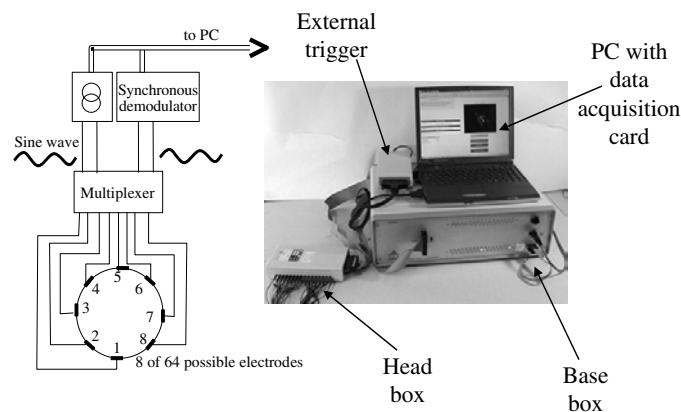


Figure 1. Schematic diagram and photo of UCLH Mk1b.

the current source from the receive amplifier, which minimizes the effect of imbalance in the current source outputs (Cusick *et al* 1994).

It is desirable to apply all the frequencies simultaneously to avoid temporal sampling errors due to impedance changes associated with the cardiac and respiratory cycles. In addition to our UCLH Mk1b system described above, several other recent EIT systems record at a single frequency, selectable from a range, typically from 10 kHz to 2 MHz (Cook *et al* 1994, Zhu *et al* 1994, Hartov *et al* 2001, Yerworth *et al* 2001). A group in Sheffield, UK, has produced an EIT system which records at many frequencies simultaneously. Their latest design is the Sheffield Mk3.5 (Wilson *et al* 2001). This is a parallel system which is based on eight or more standalone modules, in order to avoid the need for a multiplexer. Each module is connected to a pair of electrodes, each of which is shared with a neighbouring module. Drive current is applied as a composite waveform, which contains ten sinusoidal frequencies simultaneously. Three such waves are rapidly applied sequentially, to give a total of 30 frequencies from 2 kHz to 1.6 MHz. The resulting voltages are decomposed into the magnitude and phase of the individual frequencies using a dedicated digital signal processor on each module (Texas Instruments '549 DSP). Each parallel voltage dataset for a single application of these 30 frequencies is collected in 5 ms, so that 25 complete image sets are produced per second with eight electrodes (figure 2).

In general, the direction of the Sheffield group has been to use fewer electrodes with the aim of characterizing tissue rather than having a high spatial resolution. The experience in the UCLH group in developing head EIT has directed us to aim for as high a spatial resolution as possible, which requires 32 or more electrodes. Theoretically, a large number of the Sheffield Mk3.5 modules could be used, which would produce a fast, parallel system, but this would require that the system were hardwired for a pre-set protocol. In the future, this could be optimal but, at present, it is desirable to retain the ability to vary the electrode selection protocols for testing purposes and different clinical situations, such as neonatal, as opposed to adult, use. In addition, a parallel system would be large and much more expensive.

We therefore elected to design a new system which combines features of both the Sheffield Mark 3.5 and UCLH Mk1b systems, for producing rapid simultaneous multifrequency images of brain function. This employs a single current/receive module from the Sheffield Mark 3.5 with the addition of cross-point switches, as used in the UCLH Mk1b, for selection of drive and receive electrodes. In principle, use of the cross-point switches might be expected to introduce stray capacitance and introduce measurement error. This effect has been assessed

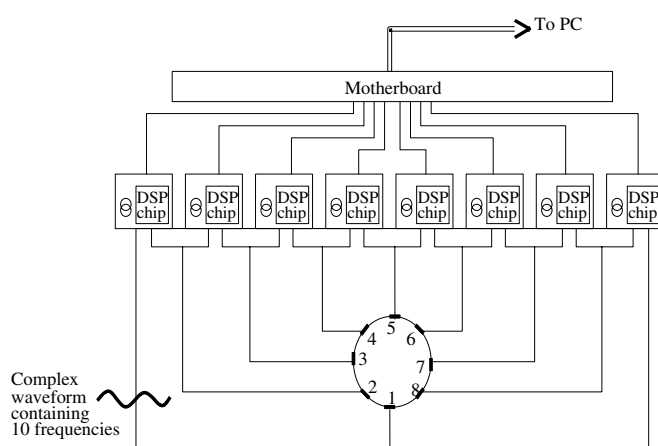


Figure 2. Schematic diagram of Sheffield Mk3.5.

by comparing the electronic performance of the new system and its accuracy in imaging biological samples in saline filled tanks. The purpose of this paper is to present the design and assess whether any consequent effect on performance can be justified in terms of the practical advantages of a multiplexed system.

2. Design of the new system

In many EIT designs, current is injected through adjacent pairs of electrodes, which gives rise to the greatest spatial resolution (Brown *et al* 1999, p 391). Unfortunately, little current enters the brain, which is the region of interest, as the skull is highly resistive and diverts current through the conductive scalp. Sensitivity to impedance changes in the brain is maximized if the current is injected through pairs of electrodes which are as far apart as possible (Tarassenko *et al* 1985, Bayford *et al* 1996). This is termed 'diametric current drive'.

The Sheffield Mark 3.5 system is hardwired for adjacent current drive and only has eight electrodes and so is not suitable for head imaging without modification. However, the individual modules used for each electrode pair are of a high specification and we elected to use a single one of these as the basis of a dedicated head imaging system. We also designed the system so that it was physically small and suitable for use on wards and intensive care units, where space is at a premium.

2.1. Cross-point switches and associated capacitance

The capacitance to ground of cross-point switches (50 pF typically for a low capacitance device), reduces the bandwidth of EIT systems, because this, coupled to the series complex impedance of skin–electrode interface, acts as a low-pass filter (Boone and Holder 1996). This is not a significant problem with the UCLH Mk1b because it operates over the relatively low frequency range of 225 Hz to 77 kHz (Yerworth *et al* 2002), but might be expected to limit bandwidth with the Sheffield Mk3.5, which applies currents with frequencies up to 1.6 MHz. Theoretically, this capacitance could be cancelled out by placing a negative impedance converter (NIC) on each lead (Horowitz and Hill 1989). We attempted this in preliminary experiments, but elected to omit these, as they were difficult to stabilize and did not confer significant improvements in performance over the frequency range tested. The permittivity of blood is approximately constant up to 500 kHz whereas that of grey matter

falls by a factor of 20 between 2 kHz and 500 kHz (Gabriel *et al* 1996a, 1996b). We therefore accepted a reduced bandwidth of 1 MHz as likely to be sufficient for brain imaging with the new system.

2.2. Screened leads

Unlike the UCLH Mk1b, the Sheffield Mk3.5 was designed to use triaxial screened leads because it operates at a higher bandwidth. Our proposed system was designed to address 64 electrodes. Such leads to 64 electrodes would have required extra screen drivers and the weight and bulk of such cables hanging from the head would have reduced patient comfort and increased the likelihood that electrodes would be pulled off.

We therefore implemented a novel design in which the cross-point switches were mounted much closer to the head, on a specially designed fabric headnet. Unscreened leads, about 10 cm long were used to connect the cross-point switches and the electrodes. Thus only four screen drivers were needed. With this design, only five cables—the four triaxial leads and a serial cable for control of the cross-point switches—were now needed to connect the main box and the cross-point switches on the electrode headnet.

2.3. Electrode charging

Transient errors of up to one hundred per cent, lasting tens of seconds, in the measured voltages were initially observed, due to charge accumulation at the skin–electrode interface. A first-order high-pass filter, with a cut-off frequency of 1 kHz, was inserted into each electrode line. This permitted any built up charge to discharge to ground, and no significant error due to this mechanism was subsequently observed.

3. Methods

A single channel Sheffield Mk3.5 single channel system was modified to add a serial control output port, linked to the on board Digital Signal Processor (Texas Instruments '549 DSP). Two (of a possible four) cross-point switch (MITEL MT8816) boards were built according to the UCLH MK1b design. Each such board served 16 electrodes and had a high-pass filter on each channel. These were connected, in parallel, to the set of triaxial leads supplied with the Sheffield Mk3.5 System (figure 3).

The performance of this new system, the UCLH Mk2 (figure 4), has been compared with the two parent devices and its ability to image test objects within saline filled tanks assessed as follows. Where data have been normalized, this has been done by expressing the raw boundary voltages for each image dataset as a percentage change from those for the reference image specified.

3.1. Bandwidth of analogue circuitry

The passive bandwidth of an EIT system is largely determined by the effective capacitance to the ground of the electrodes, which is dependent on the stray capacitance of the circuit components, the circuit board tracks and cabling. The Sheffield Mk3.5 and the UCLH Mk2 EIT systems were compared by recording the frequency at which an externally applied voltage, measured externally, reduced by 3 dB from its amplitude at 1 kHz (figure 5). The measurement was performed for the drive and receive terminals independently and the worst of these two measurements taken as the bandwidth of the system.

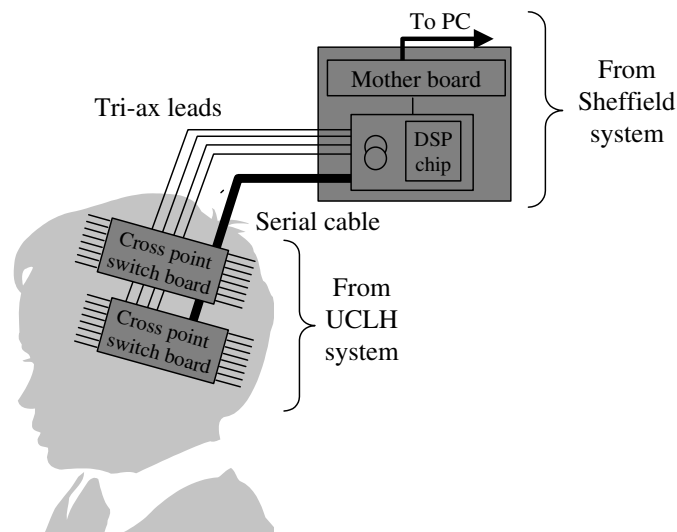


Figure 3. Schematic diagram of UCLH Mk2 system.

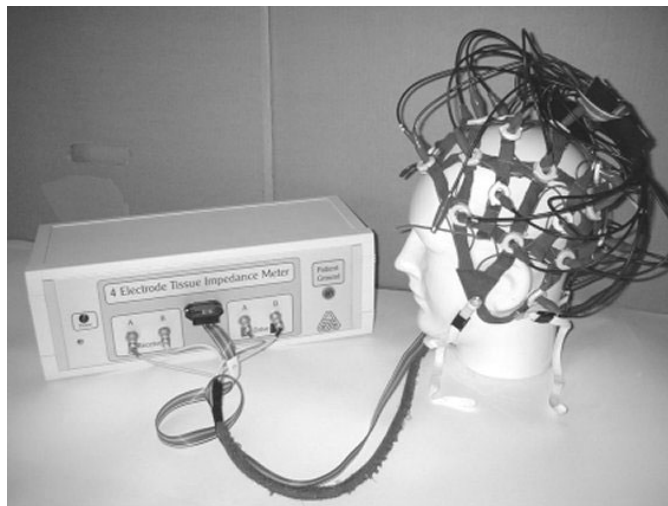


Figure 4. Photo of UCLH Mk2 system.

3.2. Noise

For each system, the root mean square (RMS) noise value was calculated from the boundary voltage data for 200 image frames, collected using eight electrodes from a cylindrical tank, 9 cm in diameter, filled with 0.2% saline. The data were corrected for linear baseline drift and then normalized to the mean value for all the datasets.

3.3. Common mode rejection ratio (CMRR)

Two circuit configurations (figure 6) were used to obtain the CMRR for each system for all available frequencies. The common mode voltage (V_{cm}) and the differential voltage (V_{in}) were measured by the system under test. Since the value of V_{in} , for this circuit, would be zero

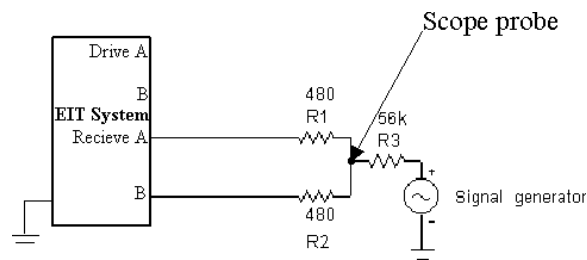


Figure 5. Bandwidth measurement circuit.

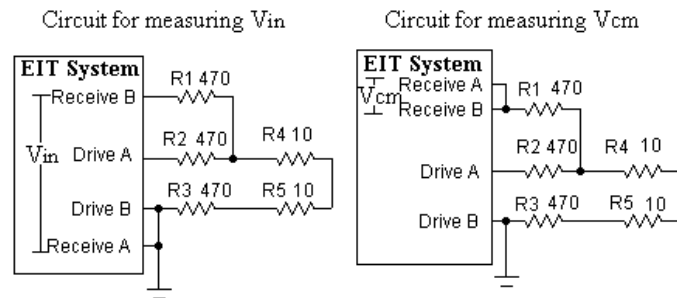


Figure 6. CMRR measurement circuits.

for a perfect system, these measurements can be used to calculate the CMRR from (Brown *et al* 1999)

$$\text{CMRR} = 20 * \log_{10}(V_{\text{cm}}/V_{\text{in}}). \quad (1)$$

3.4. 3D frequency dependent image of a piece of banana

All impedance tank measurements were made at a room temperature of 18–22 °C. A cylinder of banana was inserted into a spherical tank, diameter 20 cm, filled with 0.2% saline and imaged with the new UCLH Mk2 system and 31 Ag/AgCl disc electrodes. The dataset for each image comprised measurements with 258 out of a possible 419 electrode combinations, chosen to maximize distance between drive pairs, so that most drive pairs electrodes were diametric or near diametric (Tidswell *et al* 2001). Final images (figure 9) were the average of 60 datasets of the modulus of the impedance recorded over 30 s. All frequencies were recorded and the data were normalized to the average of the two datasets recorded at 250 kHz and 320 kHz. Reconstruction was performed with a truncated singular value decomposition (TSVD) based algorithm, which employed a forward model of the analytical solution for a homogeneous sphere (Gibson 2000).

3.5. Extraction of spectral characteristics from images

Data were collected from a cylindrical tank, diameter 20 cm, height 2 cm filled with 0.2% saline, into which were placed cylinders of banana, cucumber and Perspex 2 cm in diameter and 2 cm high. Two types of image were reconstructed. (1) Time difference. Images were reconstructed of the difference in the magnitude of the impedance between saline only, and saline with the test objects in place, collected at 640 kHz. (2) Frequency difference. The real and imaginary parts of the data were separately reconstructed for each frequency, normalized

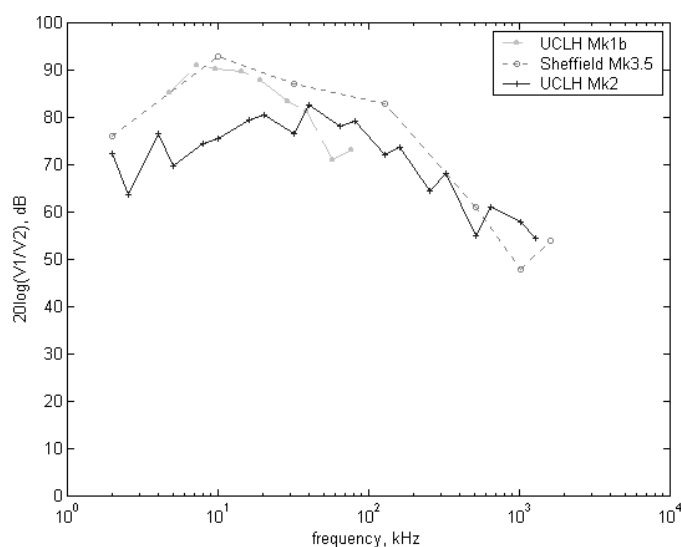


Figure 7. CMRR as a function of frequency for the three systems.

with respect to the modulus of the complex impedance at 4 kHz and 8 kHz. The image impedance spectra were derived from the reconstructed images at the peak of the impedance change due to each material (banana, cucumber, Perspex and saline), as determined by eye. The impedances of the banana, cucumber and Perspex were measured directly with the UCLH Mk2 system in single channel mode, without the cross-point switches attached. One drive and one receive electrode were connected to each end of the cylindrical sample with 1.5 m long triaxial leads and measurements of impedance were made at the same thirty frequencies used for imaging. Electrodes were Ag/AgCl discs, 9 mm in diameter. The impedance of the cucumber was also measured with an HP 4284A impedance analyser (Hewlett Packard, www.hewlettpackard.com) in two terminal modes and with the electrodes.

Cole–Cole plots were produced for each material from the image and direct data.

4. Results

4.1. Bandwidth of analogue circuitry

Sheffield MK3.5:	>1.6 MHz
UCLH Mk2:	0.8 MHz

4.2. Noise

All three systems had signal to noise levels of less than 0.3% across the centre of their frequency spectrum, 7.2–38.4 kHz for the UCLH Mk1b and 8 kHz–0.8 MHz for the Sheffield Mk3.5 and UCLH Mk2.

4.3. Common mode rejection ratio (CMRR)

The CMRR for each system decreased as a function of frequency (figure 7); that of the UCLH Mk2 system was about 10 dB less than the Sheffield Mk3.5 and UCLH Mk1b at 1 kHz.

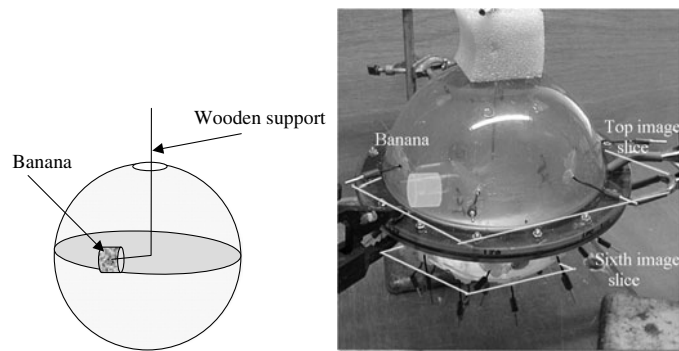


Figure 8. Position of banana portion in saline filled tank, (a) schematic, (b) photo with image planes overlaid.

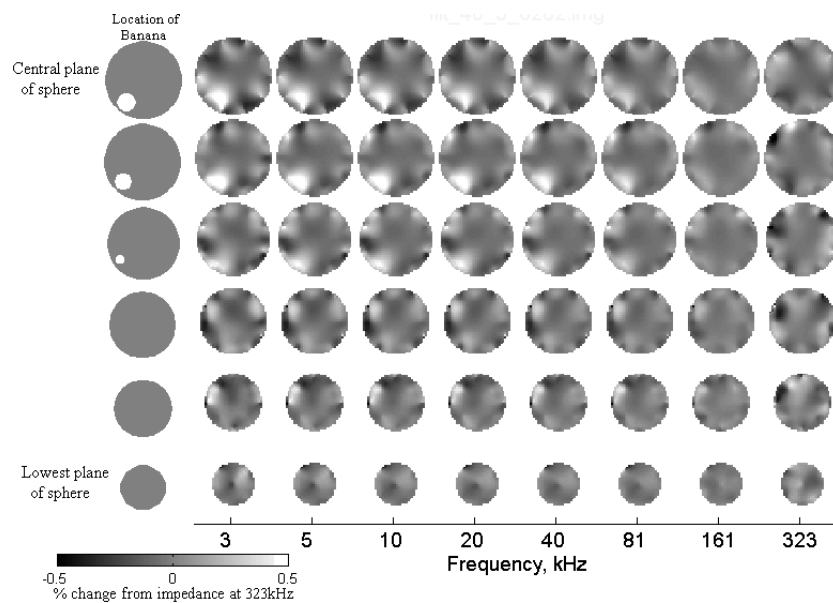


Figure 9. Banana portion in saline filled tank.

4.4. 3D frequency dependent image of a piece of banana

An area of increased impedance, corresponding to the true position of the banana in the tank, was visible at all frequencies below 81 kHz (figures 8 and 9).

4.5. Extraction of spectral characteristics from images

In the time difference images, impedance changes corresponding to the true position of all three samples were evident; the Perspex showed the largest contrast. In the frequency difference images, the impedance changes corresponding to the true position of the cucumber and banana were again evident, but the Perspex was not clearly apparent. This is consistent with the frequency dependent impedance characteristics of Perspex, which is an insulator and so has negligible conductance at all the frequencies recorded (figure 10).

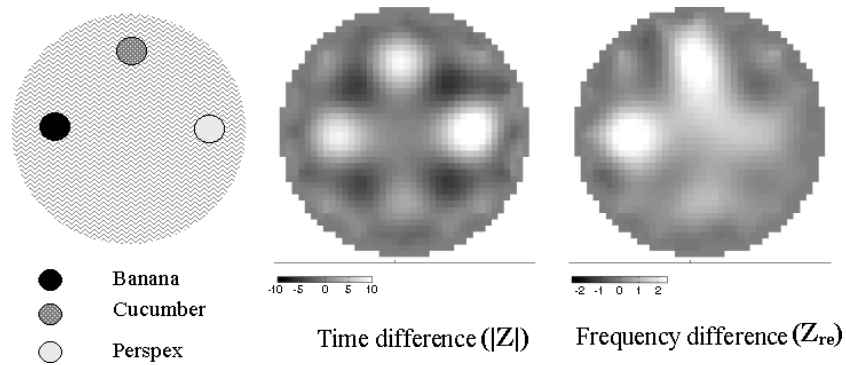


Figure 10. Effect of normalizing data with respect to time and frequency.

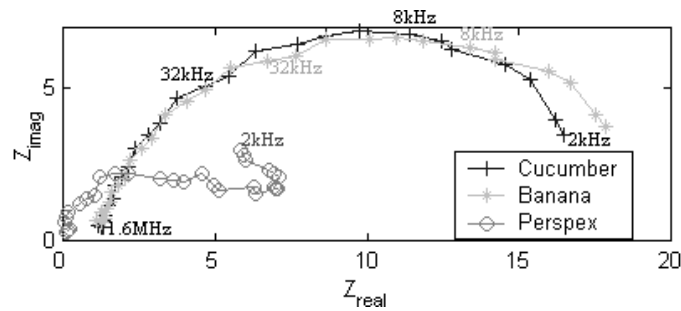


Figure 11. Cole-Cole plot on individual samples.

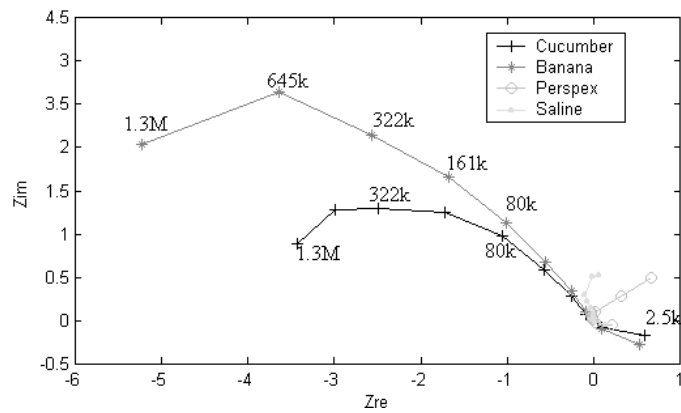


Figure 12. Cole-Cole plot of data extracted from image reconstructions. (Impedance values are in arbitrary units relative to the impedance at 4 kHz).

In direct measurements, banana had a centre frequency (f_c) of 25 kHz and cucumber 13 kHz, which matched the centre frequency obtained from the HP Analyser measurements. Plots derived from the reconstructed images had centre frequencies of 322 kHz and 628 kHz for banana and cucumber respectively, which were substantially larger than those measured directly. However, both plots were roughly semicircular, and the ratio of the centre frequency of banana to cucumber was double in both cases (figures 11 and 12).

5. Discussion

5.1. Comparison of data quality between the three systems

Combining the two original systems, Sheffield Mk3.5 and UCLH Mk1b, did not increase noise although, as expected, the bandwidth and CMRR of the UCLH Mk2 system were slightly reduced compared with the original Sheffield Mk3.5 system.

This bandwidth reduction was probably because of the additional capacitance associated with the cross-point switches. Theoretically, this could be reduced if NICs were used. However, since we found a high risk of system instability associated with the use of these, we have not employed these in the design.

A common mode signal is an important problem in EIT measurement (Boone and Holder 1996). This largely occurs because applied current is not perfectly balanced and some of it is driven through the high input impedance of the receive amplifiers. It is made worse by stray capacitance, and hence by the use of cross-point switches. In the UCLH Mk1b, the problem was addressed by separating the ground planes of the drive and receive circuits, so that the drive circuit was as isolated as possible. The Sheffield Mark 3.5 had a common ground plane and relied on maximum common mode rejection by careful selection of electronic components. In the UCLH Mk2 system, the CMRR was degraded, probably because we were not able to separate the ground planes of the drive and receive circuits and the cross-point switch will have introduced significant stray capacitance. However, the resultant CMRR is only 10 dB less than the Sheffield MK3.5. The effect on image quality of this is a matter for empirical testing, and was the rationale for tank testing in this study. However, its true effect will only become apparent in clinical studies, where there are large skin–electrode interface impedances. If this does cause a significant degradation in clinical data, we will have to consider redesigning the Sheffield Mk 3.5 drive/receive module to allow separation of drive and receive circuits.

5.2. Ability of new system to image biological materials

Regions of different complex impedance could be clearly distinguished within a tank in the three-dimensional frequency difference image of a banana, without reference to an image of the tank containing only saline (figure 9). This is similar to the imaging problem in the human head, and is encouraging to the view that the compromises made in the design were justifiable. The system performance has also been validated by the ability to extract the spectral characteristics of regions of interest from reconstructed images (figure 12). For each material, the plots of spectral response obtained by all three methods have a similar shape, although those extracted from the reconstructed data had substantially shifted centre frequencies. The reconstruction algorithm employed in these reconstructions was designed for reconstruction of the modulus of the impedance at a single frequency and so its use for separate reconstruction of real and imaginary data represents a significant simplification. The data are also normalized with respect to frequency, so that the shape and angle of the curve may be shifted. The Cole–Cole plot derived from the image data is therefore presented as empirical data, and cannot be directly compared with the directly measured impedance properties. Ultimately, we plan to improve the reconstruction algorithm to enable direct reconstruction of complex impedance data; however, it may be that the empirical use of this simplified approach may still yield empirical data which may be used clinically to distinguish different conditions in the brain. The difference between the direct and imaged data may of course have also been due to instrumentation errors introduced by the multiplexer and the use of data from many electrode combinations in image reconstruction.

5.3. Finding the balance between practicality and signal quality

The design decisions that were made in order to reduce the size of the system and the weight and bulk of leads which hang from the head have, as expected, somewhat degraded the performance of the system, with respect to the original Sheffield Mk3.5. However, the deviation from ideal system performance was relatively small and still enabled clear images to be obtained in the tank studies. Although clinical testing has still to be performed, our current view is that we have struck a reasonable balance between practicality and performance. Data would be greatly degraded in practice if electrodes pulled off under the weight of their leads. It would also be more difficult to obtain the cooperation of potential subjects and clinical staff if they were confronted with a large system that would weigh them down or impede their clinical activities.

5.4. Conclusions

We have developed an EIT system to meet the specific requirements for measurement of frequency referenced impedance changes within the human head. The system has been validated with tank studies and is ready to be used in preliminary clinical trials although further improvements to signal quality and image reconstruction will be sought.

There are several EIT systems currently available for clinical use, but we believe that this design differs in certain key respects, which makes it ideally suited for our intended purpose of imaging brain function in ambulant subjects. We have retained the design of the UCLH Mk1b, in which the patient hardware is light and can move with the subject. While this was originally designed for ambulant patients on an EEG telemetry unit, it also makes the system much more acceptable in crowded clinical departments, such as the adult or neonatal ITU. At present, we are not aware of any studies that have resolved the issue of the optimal number of electrodes to use, especially for the approximately spherical geometry of the head. The use of a multiplexer will allow us to examine whether the adoption of 64, or even 128, electrodes, confers tangible benefits in image resolution. It also will allow us experimental flexibility to settle on optimal electrode combinations. With more electrodes, compromises will need to be made to the goal of maximizing the separation of current drive electrodes, and using as many as practical of the possible combinations. Once this is settled, we may retain this multiplexer design, or move to one more closely related to the original Sheffield Mark 3.5 concept, in which there were many parallel channels, hardwired to a pre-set configuration.

Planned clinical trials will include the study of patients presenting with acute stroke with the aim of differentiating ischaemic or haemorrhagic types. We also plan to use this to develop studies during seizures in adults and evoked activity and seizures in neonatal units currently performed at a single frequency over time. EIT has many practical advantages in these conditions and we are excited by the prospect of determining the extent to which multifrequency recording could improve the ability of EIT to provide a robust new imaging method and allow it to enter into routine clinical use.

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