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NOTE

Drive and measurement electrode patterns for electrode impedance tomography (EIT) imaging of neural activity in peripheral nerve

J Hope1,3 ©, F Vanholsbeek2,3 © and A McDaid1 ©

1 Department of Mechanical Engineering, The University of Auckland, 5 Grafton Road, Auckland 1010, New Zealand
2 The Department of Physics, The University of Auckland, 38 Princes Street, Auckland 1010, New Zealand
3 Dodd Walls Centre for Photonic and Quantum Technologies, New Zealand

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Abstract

Objective: To establish the performance of several drive and measurement patterns in EIT imaging of neural activity in peripheral nerve, which involves large impedance changes in the nerve’s anisotropic length axis. Approach: Twelve drive and measurement electrode patterns are compared using a finite element (FE) four-cylindrical shell model of a peripheral nerve and a 32 channel dual-ring nerve cuff. The central layer of the FE model contains impedance changes representative of neural activity of −0.30 in length axis and −8.8 × 10⁻⁴ in the radial axis. Six of the electrode patterns generate longitudinal drive current, which runs parallel to the anisotropic axis, while the remaining six patterns generate transverse drive current, which runs perpendicular to the anisotropic axis. Main results: Of the twelve patterns evaluated, transverse current patterns produce higher resolution than longitudinal current patterns but are also more susceptible to noise and errors, and exhibit poorer sensitivity to impedance changes in central sample locations. Three of the six longitudinal current patterns considered can reconstruct fascicle level impedance changes with up to 0.2 mV noise and error, which corresponds to between −5.5 and +0.18 dB of the normalised signal standard deviation. Reducing the spacing between the two electrode rings in all longitudinal current patterns reduced the signal to error ratio across all depth locations of the sample. Significance: Electrode patterns which target the large impedance change in the anisotropic length axis can provide improved robustness against noise and errors, which is a critical step towards real time EIT imaging of neural activity in peripheral nerve.

1. Introduction

Electrical Impedance Tomography (EIT) is an imaging modality using electrical impedance as the contrast agent. Biomedical applications of EIT include monitoring of respiratory and pulmonary systems [1], identification of ischaemic brain tissue for diagnosis of stroke [2], and localisation of epileptic foci [3, 4] amongst others [5]. Differential EIT imaging of neural activity, ‘neural-EIT’, is made possible by transient changes in tissue impedance attributable to increased ion flux across neurone and axon membranes during neural activity [6]. The application of neural-EIT to a nerve cuff is an emerging field which offers a potential means to classify multiple concurrent compound action potentials within a peripheral nerve for neural prosthetics [7]. It is common in biological applications of EIT to configure the drive and measurement electrodes on the same plane in a ring around the sample boundary, which is then expanded to 3D EIT by stacking several rings, or 2D imaging planes [8–11]. Where stacked rings are not practical, such as half ellipsoid on the head, drive and measurement pattern strategies are employed to target a region of interest [12–16] and maximise information produced [17]. In a multi-contact nerve cuff the electrodes are configured in rings around the outer boundary of the nerve [18–20], which can be modelled as the surface of a cylinder [20]. EIT simulations by [21], for 3D EIT lung imaging of the thorax, compared seven possible drive EIT current and measurement patterns within a dual-ring electrode array comprised of two rings of eight electrodes. The authors modelled the lung and thorax as a...
cylindrical sample volume with isotropic conductivity features, and tested both longitudinal and transverse current patterns, concluding that transverse current patterns provided the best performance in presence of noise and electrode placement errors. The same seven current patterns, concluding that transverse current features, and tested both longitudinal and transverse cylindrical sample volume with isotropic conductivity measures on a cylindrical isotropic phantom and on the tank phantoms, was performed by [21], concluding that an electrode pattern with a sequence of alternating transverse and longitudinal currents, called ‘Square’, provided the best performance. A comprehensive modelling study of all possible transverse current patterns in ring of 16 electrodes, with validation on saline tank phantoms, was performed by [23], concluding that pairing drive and measurement electrodes at one electrode spacing less than 180 degrees is optimum.

The results in [21] and [22] assumed an isotropic sample, and so aren’t directly transferrable to peripheral nerves because the region of interest for EIT, the nerve fibres, are highly aligned along the nerve length axis, producing electrical anisotropy. This fibre alignment, together with the fibre cytostructure, produces a fraction change in impedance during neural activity which is significantly higher in longitudinal direction, parallel to the fibres, than in the transverse direction, across fibres, as predicted by models of unmyelinated and myelinated fibres [7], and observed in in-vivo experiments [24]. Furthermore, the presence of anisotropy can produce boundary voltage data with non-unique solution [25], although numerical methods with some a-priori information have proven capable of reconstructing anisotropic anomalies in 2D simulations [25–27] and in 3D simulations to manage anisotropy of white matter in the brain [28, 29]. Transverse current patterns in a nerve would largely eliminate the anisotropy by operating in a plane perpendicular to the axis containing the unique conductivity (the ‘anisotropic axis’), an approach adopted by [30] on peripheral nerve and by [31] on muscle tissue. However, because transverse current in a nerve is subject to a lower fraction change in impedance during neural activity, it suffers from a critically low signal to noise ratio [24]. Researchers typically circumnavigate this problem by averaging recordings across multiple measurements in order to reduce noise [17, 24, 30, 32], a practice which hinders real time neural-EIT. There is, therefore, a need to investigate whether the large impedance change in the longitudinal, anisotropic axis improves the signal to noise ratio of longitudinal current electrode patterns, and whether operating in the presence of anisotropy produces any detrimental effects on EIT reconstruction.

In this study, we present eight drive and measurement electrode patterns selected to contain either the maximum or minimum angular offset between electrode pairs. The electrode patterns are implemented, for the first time, on a finite element (FE) model of a four-shell cylindrical sample with anisotropic conductivity along the length axis of the central shell.

| Layer               | Conductivity (S/m) | Radius (μm) |
|---------------------|--------------------|-------------|
| Intra-fascicle tissue | 0.08757            | 545         |
| Perineurium          | 0.021              | 550         |
| Epineurium           | 0.08257            | 600         |
| Saline              | 2                  | 680         |

Performance is evaluated using several quantitative metrics as well as a qualitative analysis of the reconstructed conductivity map. The results highlight the influence that the anisotropic impedance characteristics of the neural environment have on the performance of electrode patterns. The study is designed with specific interest in neural-EIT of peripheral nerves, although the results are relevant to any cylindrical sample with anisotropic length axis e.g. muscle.

2. Methods

2.1. EIT forward solution

Solutions to the EIT forward problem were obtained using a cylindrical shell model approximation of a 50 mm length, single fascicle, sciatic nerve of rat as described in [7], table 1. The intra-fascicle tissue was divided into a grid of 49 sub-volumes each extending the length of the nerve, figure 1(a). The number of sub-volumes was selected to produce a spatial resolution comparable to that of high density penetrating electrode arrays such as the UTAH slanted micro-electrode array [33], considered a high spatial resolution neural interface. The grid pattern of the sub-volumes, with the majority of sub-volumes evenly sized and spaced at regular intervals in the lateral axes, is similar to that in [34] and facilitates spatial analysis of some performance metrics independent of the size and shape of conductivity feature. The grid pattern produced 4 sub-volumes, in the top/bottom left/right corners of the intra-fascicle volume, which were significantly smaller than the remaining sub-volumes and so were excluded from analysis and reconstruction.

The nerve cuff with dual-ring electrode array contained two rings of 16 electrodes, each 1.1 \( \times \) 0.11 mm in size, arranged into on a 22.5° pitch around the circumference. Electrodes were implemented with the complete electrode model (CEM) [35], including a contact impedance of 1.5 \( \times 10^{-4} \) Ωm² at the electrode-saline interface and an electrode conductivity of 4 \( \times 106 \) S m⁻¹. Simulations were run with the two electrodes rings spaced at 3 mm, 6 mm and 10 mm apart along the nerve length. All external surfaces were insulated.
The FE model was implemented in COMSOLMultiphysics version 5.3, using Electric Currents physics in the AC/DC module, on a Dell Optiplex 7040PC with Intel i7-6700 processor. Meshing was performed with minimum mesh size of 0.1 mm, a max growth rate of 1.3, a curvature factor of 0.2, and a resolution of narrow regions of 1, producing a total of 750 k free tetrahedral elements with minimum and average mesh quality of 2.8 × 10⁻² and 0.54 respectively. The FE model was then solved for each drive and measurement pattern with a 10 μA amplitude drive current applied between each of the 16 drive electrode pairs one pair at a time, with the remaining electrodes acquiring boundary voltage measurements. A quasi-static approximation of Maxwell’s equations was used to implement neural activity by solving the FE models under several static conditions, where, for each condition, the electrical conductivity of fascicle sub-volumes was set to that of either the active or inactive state. This quasi-static approach is valid up to several 100 s of kHz for intra-fascicle tissue [7].

2.2. EIT inverse solution
Zeroth order Tikhonov regularisation was used to invert the sensitivity matrix, as was done in [17, 34], with the Tikhonov regularisation parameter selected using the L-curve, or Pareto frontier curve, method [36]. To replicate real operating conditions, we synthesised data in line with recommendations provided in [33]; these are: (1) to use a smaller mesh size: minimum 0.05 mm, resulting in 4.3 M free tetrahedral elements with minimum and average mesh quality of 7.0 × 10⁻² and 0.60 respectively; (2) ensure different size, shape and location of conductivity features: 3 fascicle model with 90 μm thick epineurium, figure 1(b); (3) add either low (+/−0.35 μVRMS) or high (+/−35 μVRMS) Gaussian noise to each measurement; (4) add random hardware error to each electrode (channel): within either a low (+/− 1 μV) or high (+/−100 μV) range; and (5) quantization: either low (1 μV) or high (10 μV) rounding. All low noise, error and quantization conditions were applied together, as were all high conditions.

Noise and errors were selected as absolute values which are independent of the magnitude of the boundary voltages. In practice, some error sources are dependent on the signal size, such as noise in the drive current and electrode impedance measurement errors, whereas others are independent of signal size, such as noise and accuracy in the ADC hardware.

2.3. Drive and measurements patterns
Twelve drive and measurement patterns were investigated: six utilising longitudinal current, implemented in a dual ring electrode array, and six utilising transverse current, implemented in a single-ring electrode array. In each pattern, current flows between the drive electrode pair, and the remaining electrodes are paired up to produce differential measurements. In both transverse and longitudinal drive currents maximum and minimum angular offsets in drive electrode pairs were selected, respectively, to minimise or maximise current channelling through the low resistance outer fluid layer [37]. An intermediate angular offset, of 157.5 degrees, was selected due to the recommendation for transverse currents in [23] to pair electrodes at one electrode spacing less than 180 degrees, which we also applied to longitudinal current.

With longitudinal current, drive and measurement electrode pairs were on different electrode rings and with angular offset of 0, 157.5, or 180 degrees, figure 2(a). We combined the longitudinal drive and measurement patterns following the convention in [21] to produce three possible patterns (drive/measurement angular offset in degrees): 0/0, 157.5/157.5, and 180/180, as well as in a non-conventional manner to produce three further patterns: 0/180, 0/157.5, and 180/157.5. Switching around the angular offsets applied to the drive and measurement pairs was found to produce equivalent results in [23], e.g. 180/0 is equivalent to 0/180. Therefore, symmetrical patterns were not investigated in the current study. Of the
Table 2. Condition number of the sensitivity matrix for each drive and measurement electrode configuration.

| Electrode ring spacing | N/A   | 3 mm  | 6 mm  | 10 mm |
|------------------------|-------|-------|-------|-------|
| Longitudinal: 0/0       | 1.57E + 6 | 3.07E + 6 | 1.34E + 6 |
| Longitudinal: 180/157.5 | 3.53E + 6 | 4.56E+6  | 8.10E + 6 |
| Transverse: 22.5/22.5   | 3.04E + 4 |         |       |       |
| Transverse: 157.5/157.5 | 4.18E + 5 |         |       |       |
| Transverse: 180/180     | 4.57E + 5 |         |       |       |
| Transverse: 157.5/22.5  | 1.74E + 5 |         |       |       |
| Transverse: 180/22.5    | 1.71E + 5 |         |       |       |
| Transverse: 180/157.5   | 3.07E + 5 |         |       |       |

longitudinal current configurations studied here and longitudinal current configurations studied here Longitudinal: 180/180 featured in modelling and tank phantom studies by [21, 22] under the name 'Zigzag-opposite'.

With Transverse current, drive and measurement electrode pairs were on the same ring and with angular offsets of either 22.5, 157.5, or 180 degrees, figure 2(b). Again, we combined the drive and measurement to produce six possible patterns (drive/measurement angular offset in degrees): 22.5/22.5, 157.5/157.5, 180/180, 22.5/180, 22.5/157.5, and 180/157.5. Of the transverse current configurations studied here Transverse: 180/180 and Transverse: 22.5/22.5 patterns were both evaluated in [21, 22] under the names 'Planar-opposite' and 'Planar' respectively; and all patterns featured in a modelling and tank phantom study by [23].

2.4. Performance metrics

Electrode patterns were compared using three criteria: (1) analysis of the condition number together with singular values from the singular value decomposition (SVD) of the sensitivity matrix; (2) the signal to error ratio, which we define as:

\[ SER = 20 \log(\frac{v_e}{v_r}) \]  

where \( v_e \) is the standard deviation of the normalised differential boundary voltage measurements obtained from all 16 drive electrode pair conditions, and \( v_r \) is the maximum possible voltage error from noise and hardware errors normalised using the mean of differential measurements from the inactive state. This formulation of the SER is similar to the 'distinguishability' metric defined in [23] in that both place more emphasis on the values least affected by noise through use of the Euclidian norm, in the case of SER through the formula for standard deviation; (3) qualitative analysis of the reconstructed conductivity map, where poor quality reconstruction includes conductivity changes in wrong locations and/or significantly smaller in magnitude.

3. Results

Inspection of the sensitivity matrix for Transverse: 180/180 pattern revealed normalised boundary voltage measurements were several orders of magnitudes larger on the electrode pair at +/−90 degrees positions relative to the drive current electrode pair (i.e. on the left and right hand sides in figure 2(b)) due to symmetry of the circular sample cross section. Differential boundary voltages of negligible magnitude produced a negligible mean value, which in turn distorts the normalised boundary voltages through its calculation as the difference divided by the mean.
Measurements from this electrode pair were therefore excluded from the sensitivity matrix.

Longitudinal patterns exhibited minimal difference in condition numbers, where large condition numbers indicate a more ill-conditioned sensitivity matrix, and in singular values, table 2 and figure 3(a) respectively. The same was true of the condition numbers for transverse patterns, while with singular values the patterns containing 22.5° angular offset in drive electrode pair were all noticeably higher than those containing 157.5° and 180° angular offsets, figure 3(b). In comparing longitudinal and transverse patterns: condition numbers were

**Figure 3.** Normalised singular values, from singular value decomposition of the sensitivity matrix, for each longitudinal current (a) and transverse current (b) electrode pattern, with 6 mm ring spacing in longitudinal current patterns.

**Figure 4.** The signal to error ratio (SER) at each grid index for longitudinal electrode patterns of 10 mm, 6 mm and 3 mm ring spacing (a), and for transverse current patterns (b). The grid in the single fascicle nerve model are shown overlaid with the corresponding grid index in (c).
consistently higher and singular values were consistently lower in longitudinal patterns than in transverse patterns, albeit to a lesser extent with Transverse: 180/180, and Transverse 157.5/157.5. Transverse patterns appear to be, as a whole, more robust against errors relative to the signal size.

A large positive SER corresponds to high robustness against noise and error, whereas negative SERs indicate the signal standard deviation is below the specified noise and error level. With longitudinal patterns the signal standard deviation $\sigma_{e}$ from equation 1, increased with decreasing ring spacing, as did $\sigma_{e}$. The net effect was a decrease in SERs across all grid indices as ring spacing decreased, figure 4(a). With transverse patterns, 157.5/157.5 produced the highest SER across all grid indices, and 22.5/22.5 the worst, figure 4(b). In comparing longitudinal and transverse patterns: the troughs in SER plots, with minima corresponding to central grid indices 9, 16, 23, 30 and 37, figure 4(c), are significantly larger in all transverse patterns than in all longitudinal patterns, indicating that longitudinal patterns provide better sensitivity to conductivity changes in the centre of the sample. Similarly, with the quarter circle shaped fascicle active in the multi-fascicle model, a high noise and error level of 0.2 mV produced SERs of between $-5.5$ and $+0.18$ dB in longitudinal patterns with 10 mm electrode spacing, and between $-46$ and $-19$ dB in transverse patterns. The higher SERs of longitudinal patterns indicate they are more robust than transverse patterns against noise and error in voltage measurements.

Under the low noise and error conditions, EIT reconstruction of impedance changes in two quarter shaped fascicles and in one quarter-circle shaped fascicle could be distinguished from one another in all electrode patterns, figure 5(a) and (b). Under the high noise and error conditions, longitudinal patterns exhibited some additional blurring, whereas the transverse patterns were severely affected, as exhibited by significant impedance changes in significantly wrong locations, figure 5(b). Where noise did not corrupt the results, 180/180 pattern in both longitudinal and transverse currents reconstructed a ‘mirrored’ impedance distribution, such that equal magnitude impedance changes in grids on the both the correct side and opposing side of the nerve cross section were observed. The other five transverse patterns and Longitudinal: 0/0, 157.5/157.5 and 180/157.5 also produced impedance changes in grids in significantly wrong locations, although often with far smaller impedance magnitude than those grids corresponding to the correct locations. Overall, with the exception of the two 180/180 patterns, the transverse patterns appear to offer higher resolution than the longitudinal patterns, as exhibited by tighter clusters of grids with impedance change, but also a higher susceptibility to noise and errors which manifests as impedance changes in significantly wrong locations.

4. Discussion

Analysis of condition numbers and singular values predicted transverse patterns to be, as a whole, more robust against errors relative to the signal size, i.e. the normalised boundary voltages. Results of SER analysis on the transverse patterns are in agreement with findings in [23], which used a metric called the ‘distinguishability factor’. This agreement is expected because the anisotropic axis in peripheral nerve is in the longitudinal direction and so has minimal influence on transverse patterns. SER analysis and visual analysis of reconstructions both indicated that longitudinal patterns are more robust than transverse patterns against an absolute value of noise and errors, particularly in central sample locations, but offer poorer resolution. This is contrary to modelling in [21] on an isotropic sample, which predicted transverse patterns to be more robust against noise and errors. Therefore, in nerves, targeting the large fraction change in impedance in the longitudinal axis using longitudinal current outweighs the poorer performance previously observed in longitudinal patterns. The recommendation by [22] to use a ‘Square’ pattern, which combines aspects of Transverse: 22.5/22.5 and Longitudinal: 0/0, is an interesting approach, and appears to offer the benefits of both transverse and longitudinal current patterns. However, the demanding time resolution requirements of imaging neural activity may restrict implementation of additional drive electrode pairs as all pairs must be cycled through at least once within each time resolution increment.

Neural-EIT researchers who have utilised transverse patterns have typically averaged recordings across multiple measurements in order to reduce noise [17, 24, 30, 32]. The improved SER of longitudinal patterns may remove this need for averaging data and, therefore, open up the possibility of imaging neural activity in real time. Other factors to be considered when selecting between transverse and longitudinal patterns for neural EIT include:(1) the transmembrane capacitive charge transfer mechanism occurs at higher frequencies in transverse fibre orientation, allowing higher drive current frequencies [7]; and (2) the excitation threshold of fibres is higher in transverse orientation [38], allowing a higher drive current amplitudes. For the latter point, in-vivo studies on rat sciatic nerve indicate the excitation limits for longitudinal and transverse currents are 30 $\mu$A [24] and 150 $\mu$A [39] respectively. At these upper limits of current amplitude, the transverse and longitudinal patterns which had the highest SER values at 10 $\mu$ current, Transverse: 157.5/157.5 and Longitudinal: 0/0 respectively, are comparable to one another at the outer grid indices, figure 6(a), although the dips in SER at central grid indices for Transverse: 157.5/157.5, which are typical of all transverse current patterns, figure 4(b), are still significant. At 150 $\mu$A current amplitude the EIT reconstruction
with Transverse: 157.5/157.5 is not corrupted by the high noise and error conditions, figure 6(b), as it was at 10 μA current, figure 5.

All longitudinal patterns exhibited a trend of decreasing SER with decreasing electrode spacing, albeit to a lesser extent with 0/180, 0/157.5 and 180/157.5 patterns. This trend is expected to be countered by an increase in the fraction change in impedance during neural activity as electrode spacing decreases, which is predicted by modelling [7] but has not been included here in order to isolate the performance of electrode patterns from this system.
variable. The larger increase in $v_r$ than $v_c$ produces the negative trend between SER and ring spacing, and is, in part, an implication from selecting a noise value which is independent of the ring spacing. Noise sources which are dependent on the ring spacing, such as noise in the current source, would counter the observed trend.

An angular offset of 180 degrees in drive electrodes is desirable as it is reported to minimise current channeling through low resistance outer layers [37]. However, for both longitudinal and transverse currents 180/180 pattern produced significant errors in the EIT reconstruction, which is in agreement with observations in [21] and [22] on 180/180 electrode patterns—although a direct comparison is not possible in the longitudinal current case due to anisotropy in our sample. The same susceptibility to errors was not displayed when an angular offset of 180 degrees in drive electrodes was coupled, in a non-conventional manner, with a different angular offset in measurement electrode pairs.

4.1. Limitations
The model includes realistic drive current amplitude, noise levels, hardware errors, quantization, different mesh sizes and different conductivity distributions. However, inaccuracies are generated from the assumption of a homogeneous intra-fascicle tissue medium, which neglects to consider that the true direction of the current path is restricted by the cytostructure of nerve fibres, for example to enter and exit through nodes of Ranvier. The geometric assumptions, such as perfect alignment of the two electrode rings and perfectly centred nerve within the cuff, would be difficult to replicate in practice. The fascicle and nerve dimensions are chosen to approximate those of the rat sciatic nerve which allows comparison to in-vivo animal studies [30, 40] but must be scaled up in number and size, respectively, to approximate major peripheral nerves, e.g. the medial nerve, in human. The impedance change applied to intra-fascicle tissue, table 1, is artificially large as it is representative of all fibres being stimulated at the same location and time, and then dispersing across a 30 mm length of nerve before reaching the nerve cuff [7]. Larger dispersion distances [41], activity in sub-groups of fibre diameters, and asynchronous firing rates would all reduce the magnitude of the change in impedance and, accordingly, the signal. To accommodate the artificially large signal, the absolute noise and error value of 0.2 mV was selected to be a factor of 20 to 200 times greater than that commonly found in neural EIT systems [6, 17, 32]. Insulation of the outer surfaces in the FE models, as opposed to an infinite boundary, artificially increases the SERs. This effect on the SERs is minimal, <0.2 dB at each grid index, but without it, a reduction in resolution of the reconstructions is expected.

As a whole, the accuracy of the model presented here is sufficient to compare performance of electrode configurations in reconstructing impedance changes in a highly anisotropic length axis, such as in peripheral nerve.

5. Conclusion
We have identified three longitudinal current patterns, 0/0, 0/157.5 and 0/180, which are more robust against noise and errors than the evaluated transverse current counterparts, and exhibit no detrimental effects from operating in the anisotropic length axis. The large SER is a critical step towards real time imaging of neural activity using EIT, where the current practice of averaging multiple measurements to improve the SER is not practical. The two FE models, which we used to generate data for the EIT forward and inverse solutions, are provided as supplementary material to allow researchers to investigate other possible electrode patterns (stacks.iop.org/BPEX/4/067002/mmedia).

ORCID iDs
J Hope © https://orcid.org/0000-0002-1301-2049
F Vanholsbeeck © https://orcid.org/0000-0001-9653-6907
A McDaid © https://orcid.org/0000-0003-3316-7344

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