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ASSESSING HUMAN BRAIN IMPEDANCE USING SIMULTANEOUS SURFACE AND INTRACEREBRAL RECORDINGS

RADU RANTA, [a,b]* **STEVEN LE CAM,** [a,b] **LOUISE TYVAERT** [a,b,c] **AND VALÉRIE LOUIS-DORR** [a,b]

[a] *Université de Lorraine, CRAN, UMR 7039, 2 av. de la Forêt de Haye, 54500 Vandoeuvre-lés-Nancy, France*

[b] *CNRS, CRAN, UMR 7039, France*

[c] *CHU Nancy, Neurology Department, 54000 Nancy, France*

Abstract—Most of the literature on the brain impedance proposes a frequency-independent resistive model. Recently, this conclusion was tackled by a series of papers (Bédard et al., 2006; Bédard and Destexhe, 2009; Gomes et al., 2016), based on microscopic sale modeling and measurements. Our paper aims to investigate the impedance issue using simultaneous in vivo depth and surface signals recorded during intracerebral electrical stimulation of epileptic patients, involving *a priori* different tissues with different impedances. Our results confirm the conclusions from Logothethis et al. (2007): there is no evidence of frequency dependence of the brain tissue impedance (more precisely, there is no difference, in terms of frequency filtering, between the brain and the skull bone), at least at a macroscopic scale. In order to conciliate findings from both microscopic and macroscopic scales, we recall different neural/synaptic current generators' models from the literature and we propose an original computational model, based on fractional dynamics.

Key words: brain impedance, simultaneous EEG–SEEG, intracerebral stimulation, computational current source models.

INTRODUCTION

In brain electro-physiology, the widely accepted model considers currents sources embedded in the brain tissue and potential measurements using electrodes, either implanted in the brain (micro-electrodes, SEEG), placed on the brain surface (ECoG) or on the scalp (EEG). Different scales can be considered for the sources and, consequently, for the measurements, from membrane patches and single cells to synchronized neuronal populations. At the microscopic scale, current sources are considered to be the ionic channels generating sub-threshold activities or action potentials. At the macroscopic scale one assumes that the current source is the synchronized synaptic activity, produced by several geometrically aligned cells firing together. Common simplified source models at the microscopic scale are point or spherical sources, seen as monopoles, while at the macroscopic scale, dipolar sources allow simpler yet generally accurate modeling. Note that single monopolar sources do not exist, as the various current sources in the brain must cancel each other in order to respect charge conservation (as for the dipolar case, which is an approximation of a two-monopole situation). Consequently, accurate microscopic modeling implies collections of monopoles, often representing compartments of detailed neuron models (see Einevoll et al., 2013 for a review, as well as e.g. Lindén et al., 2010; Leski et al., 2013; Ness et al., 2016).

Forward problem consists in estimating the potentials in space (thus at the measurement sites) given a source model and a propagation model.[1] Starting from Maxwell equations, there is an abundant literature both for the microscopic and macroscopic cases. The main difficulty consists in correctly modeling the propagation environment, *i.e.*, the impedances between the current sources and the measured potentials. Most of the research efforts are directed toward the evaluation of the homogeneous/inhomogeneous isotropic/non-isotropic nature of the brain and head tissues or to their geometrical approximations (see e.g. Bangera et al., 2010; Hofmanis et al., 2013). In all these studies, the implicit assumption is that there is no frequency dependence of the propagation model (impedance), at least in the frequency range of interest. In other words, the environment is assumed as purely resistive (although it might have different conductivities depending on the spatial position and on the orientation of the electric field). Indirect confirmations for these hypothesis are provided by the extremely large inverse problem literature: starting from the measurements and assuming a resistive propagation, quite good source localizations are obtained, both at the microscopic scale (current source density – CSD methods, e.g. Pettersen et al., 2012) and at macroscopic scale (dipolar fit, e.g. Caune et al., 2014). Direct confirmation of the

*Correspondence to: R. Ranta, Université de Lorraine, CRAN, UMR 7039, 2 av. de la Forêt de Haye, 54500 Vandoeuvre-lés-Nancy, France.

E-mail address: radu.ranta@univ-lorraine.fr (R. Ranta).

Abbreviations: CSD, current source density; LFP, local field potentials; SEEG, stereoelectoencephalogram; ECoG, electrocorticogram; EEG, electroencephalogram; PSD, power spectral density.

[1] All along this paper, by propagation we mean electrical field propagation in the brain tissues and not axonal propagation.

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dominantly resistive environment was provided by Logothetis et al. (2007), who used an injected controlled current source in a particular geometrical setup in order to asses brain tissue impedance (which was found to have a rather insignificant frequency dependency, at about 1 dB per decade). Other studies arrived to more or less similar conclusions: in Gabriel et al. (1996) for example, even if the permittivity displays a high negative slope with respect to the frequency on the whole tested frequency band (10 Hz to 20 GHz), its influence on the absolute impedance value (and on the its phase) is negligible below 1000 Hz, as pointed out also in Bédard and Destexhe (2009) (note however that the measurement uncertainties are rather important below 1000 Hz, and even bigger below 100 Hz (Gabriel et al., 1996). Moreover, further works of the same authors (Gabriel et al., 2009) only consider the resistive part of the impedance (*i.e.*, the conductivity). Roughly the same variations were observed in two recent in vivo studies (Wagner et al., 2014; Dowrick et al., 2015), except for very low frequencies, below 100 Hz.)

An alternative model was developed at microscopic scale by Bédard et al. (2006), Bédard and Destexhe (2009, 2014). In brief, this model aims to take into account the ionic diffusion in the brain tissue and proposes a Warburg-type impedance of the propagation medium instead of the purely resistive one. Unlike in the resistive models, the brain tissue is assumed to have a complex impedance, scaling in modulus as the square root of the frequency (which yields a slope of 10 dB per decade, much higher than in previous studies). The main motivation and indirect proof for this hypothesis is that it provides an explanation for the experimentally observed $1/f$ frequency scaling of the meso and macroscopic signal power spectral densities (local field potentials, LFP) (Bédard and Destexhe, 2009; Bédard et al., 2010; Destexhe and Bédard, 2013). Recently, a more direct confirmation was proposed by Gomes et al. (2016), which uses a controlled intra-cellularly injected current source in order to determine a so-called natural impedance from which one can potentially separate the membrane impedance and the extracellular impedance.

The aim of this paper is to investigate the possible frequency dependency of the electrical field generated by a dipolar current source, at different distances from the source, at macroscopic scales (in the human brain). In this sense, our approach is quite similar to the one proposed by Logothetis et al. (2007). The main difference is that we take the problem to the whole head scale. This leads to two important consequences for the modeling: the geometry is different, as the measurement electrodes can be far from the current source site (avoiding thus possible saturation problems) and, moreover, we have to deal with extremely different tissues, with *a priori* different impedances (e.g. white/gray matter *vs.* skull bone). As it will be shown, this allows us to tackle the possible frequency dependence of the brain tissue impedance using only the measured potentials at different locations, less dependent on the precise spectrum of the injected current source.

EXPERIMENTAL PROCEDURES

Experimental setup

Our experimental setup is very similar to the one presented in Bangera et al. (2010). In brief, a current source is artificially inserted into the brain, generating thus an electrical field (electrical stimulation). Current source and sink are neighboring contacts, placed on one of the multi-contact intra-cerebral electrodes (see generic representation Fig. 1). Measuring contacts are placed on several other intra-cerebral electrodes and on the scalp surface.

Potentials can then be measured at different points in the brain and on the scalp with respect to a reference electrode placed itself on the scalp, sufficiently far from the stimulation site (reference at 'infinite' distance).

The intra-cerebral stimulations were delivered during standard presurgical evaluation of pharmacoresistant epileptic patients at the University Hospital (CHU) Nancy, France (recording and stimulation devices from Micromed, Italy, electrodes from Dixi Microelectronics, France). The patients gave their informed consent and the protocol was approved by the ethics committee of the hospital.

The procedure used in this paper was applied on several stimulation sessions (different stimulations sites, amplitudes and patients). We present here the details for one patient, but the results and the conclusions are very similar for all tested data.

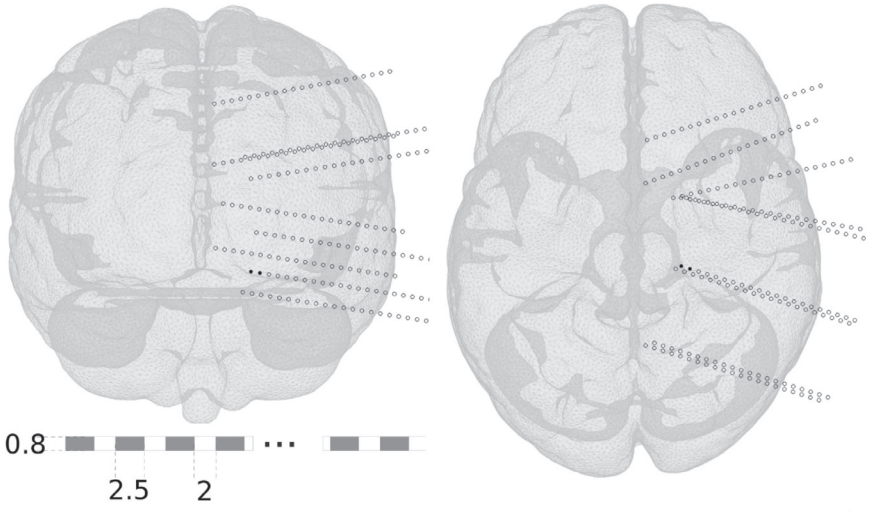

Fig. 1. Example of electrode implantation (stimulation contacts in black) and schematic representation of an intracerebral electrode (dimensions in mm).