Measuring & Inducing Neural Activity Using Extracellular Fields II: Current-source density

Mahta Sadeghzadeh
Department of Electrical and Computer Engineering, University of California San Diego
Department of Bioengineering, University of California San Diego

Abstract

Measuring and inducing neural activity in neurons using extracellular fields provides great insight into neurons functions and how they process information. This paper will consider the problem of trying to selectively sense and induce activity in neurons within a network in a living organism, using a small array of electrodes placed some distance away. One way to approach this problem is to solve for current source density (CSD) using known local field potentials. This involves solving the electrostatic forward problem where we measure the local filed potentials or low frequency part of the extracellular recorded potential by applying an equally spaced linear array or laminar electrode into the cortex [1]. The standard CSD method, involving a discrete double derivate, is then compared to inverse CSD (iCSD), where the CSD is assumed to have cylindrical symmetry and be localized in infinitely thin discs.

1. Introduction

Developing an experimental tool that enable us to induce neural activity in neurons using extracellular in vivo will provide great insight into neuron functions and process information. One approach is to measure the current source density (CSD) using laminar electrodes. This involves solving the forward problem where we measure the local filed potentials or in other words, low frequency part of the extracellular recorded potentials, which basically stem from dendritic processing of synaptic inputs, and then we can use this field potential to interpret the neural activity. There are various methods to measure and record the local field potentials, including use of equidistant linearly positioned electrodes, called laminar electrodes, penetrating through cortical layers[2]. This way we can estimate the current source density from local field potentials where either we have spatially confined cortical activity or spatially varying extracellular conductivity. Under the assumptions of homogenous in plane cortical activity, constant extracellular electrical conductivities and using equally spaced electrode contacts, we can estimate CSD from double spatial derivative using know local field potential. This standard CSD calculation method cannot obtain CSD estimates at first and last electrode due to limitation of calculation procedure. However inverse CSD (iCSD) method, which is based on the inversion of electrostatic forward solution, does not suffer from Standard CSD method's limitations.

2. Methods

Nicholson and Freeman in 1975 showed a following relationship between a current source density C(x,y,z) and extracellular field potential ϕ(x,y,z):

$$\nabla \cdot (\sigma \nabla \varphi) = -C$$

Where σ represents the electrical conductivity tensor[1]. Since we are assuming homogenous and isotropic extracellular electrical conductivity, we can assume that all the conductivity in x,y,x direction are equal to each other or in other words, σx=σy=σz=σ. In addition, we define our z-axis in a way that is perpendicular to the cortical layer while x and y-axes are defined to be in plane of the cortex. To further simplify our equations we will assume that our potential is constant in the in-plane directions so that it is only varying in z-direction:

$$\sigma \frac{\partial^2 \varphi}{\partial z^2} = -C(z)$$

The simplest method to solve for CSD is by assuming neuron current sources are evenly distributed in infinitely large planes with constant neural activity in-plane directions. Using this assumption we can simply apply the definition of the double spatial derivative to get an estimation of CSD:

$$C_{Std}(z) = \frac{\varphi(z+h) - 2\varphi(z) + \varphi(z-h)}{h^2}$$

To apply this equation, also called Standard CSD method, we will use our laminar electrode to measure the field potential at discrete set of cortical depths with a fixed spacing h. From this estimation, we can directly calculate the filed potentials by solving electrostatic forward problem.

$$\phi(x, y, z) = \frac{I_c}{4\pi\sigma\sqrt{x^2 + y^2 + z^2}}$$

Where Ic is a point current source at the origin of the infinitely large plane with homogenous and isotropic conductivity. Due to our assumption of evenly distributed current in infinite plane, this method is very limited [2].
The matrix formation of the forward solution, which is the basic idea behind the inverse CSD method, is given by:

$$\hat{C} = F^{-1}\Phi$$

Where $\hat{C}$ represents a vector containing estimated current source densities values and Φ represents a vector of local field potentials. Thus F is the N × N matrix found in the electrostatic forward calculation of extracellular potentials from known current sources. Thus with known potentials, the unknown current sources can be estimated directly from the inverse of the matrix F. In order to construct matrix F, there are three iCSD methods: δ-source iCSD method, step iCSD method and spline iCSD method that compare to standard CSD, these methods consider more general case where the current sources are evenly distributed in a cylindrical discs of some radius R [2].

The δ-source iCSD method assumes an infinitely thin circular disc with some radius R that lies in xy-plane with its center lying at *x = y = 0*. Since this circular disc basically represents a δ function in z-plane, this method is called δ-source iCSD method. Thus we can solve for potential at some height z', in terms of current source per area C_p and some radius R:

$$\varphi(z,z') = \frac{C_p}{2\sigma}\left(\sqrt{(z-z')^2+R^2} - |z-z'|\right)$$

Using this method we are basically are assuming that current source density was calculated when planar current was evenly distributed in a box of height h.

The Step iCSD method takes our previous method one step further by assuming that δ-sources are extended in the z-direction. This corresponds to having a current sources being step-wise constant in the z-direction, thus the name Step iCSD method [1]. Thus the potential measured at the center axis at position z is given by integrating the previous equation:

$$\varphi(z) = C_i \int_{z-h/2}^{z+h/2} \frac{1}{2\sigma}\left(\sqrt{(z-z')^2+R^2} - |z-z'|\right) dz'$$

It is more realistic to assume that between electrode contacts points there is a step-wise constant CSD rather than δ-source assumption. Taking the step-wise CSD method another step further, we can assume a smoothly varying CSD between CSD electrode contacts in z-direction by interpolating a set of cubic polynomials [3]. This requires that the first and second derivative of CSD in z-direction to be continuous:

$$\varphi(z') = \int_{z}^{z+h} \frac{1}{2\sigma}\sum_{m=0}^{3} a_{im}(z'-z)^m \times (\sqrt{(z-z')^2+R^2} - |z-z'|)dz'$$

The advantage of using spline iCSD method is that it assumes more realistic CSD distribution while δ-source iCSD method and step iCSD method are easier to implement.

3. Results

In case of current source density (CSD), two methods have been compared: standard CSD and one of the iCSD methods. We used δ-source iCSD method since it was easier to implement compare to step-wise CSD and spline CSD. We applied these two methods on example laminar electrode data recordings from rat barrel cortex. Ulbert et al. data was used, where they used a linear array multi-electrode with 23 contacts spaced at 0.1 mm with first electrode contact positioned at 0.05 mm below cortical surface. In addition they added oil on top of the cortical surface in order to make the surface electrically insulating [3].

The local field potential depth profile and the derived CSDs, using Standard CSD method and δ-source iCSD method are shown in Figure 1. We used color maps to plot the color-plots of the CSD. Figure 1a shows current sinks and sources when we applied Standard CSD method, while Figure 1b shows the same thing but when δ-source iCSD method was applied. In these plots we used hot colors such as yellow and red to plot current sinks or depolarizing currents and we used cool colors of blue to show current sources or hyperpolarizing currents, while the black areas represent a zero net current.

As the plots shows, Figure 1, the methods predict a dominant current sink, taking place at around 15 ms, after stimulus onset. We can see that using δ-source iCSD method allows the current to go deeper than the standard CSD method. Also iCSD method shows that at later times, weaker sink are larger and more spatially extended.

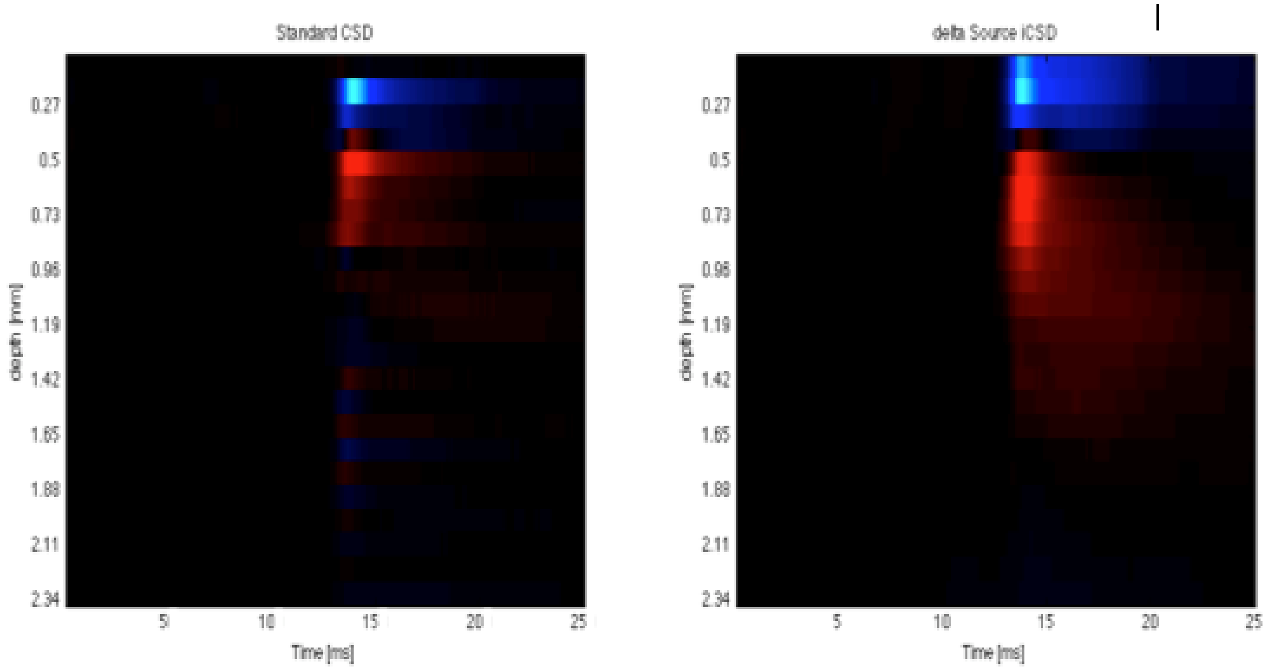

Figure 1. The local field potential depth profile and the derived CSDs, using Standard CSD method and δ-source iCSD method. (a) Shows current sinks and sources when we applied Standard CSD method. (b) Shows current sinks and sources when we applied δ-source iCSD method.

4. Discussion

As part of this project we showed that we could, by using laminar electrodes, solve for current source density (CSD) using known local field potentials. Two methods were compared to each other: Standard CSD and δ-source iCSD method.

Limitation of Standard CSD is that if we measure the field potential at N equally spaced electrode positions, we are only able find the CSD at N-2 locations since due to how we defined our three point derivative equation, we cannot estimated CSD at first and last electrode positions [2]. Therefore iCSD method is a better estimation of current source density, especially since we can use anisotropic or spatially varying extracellular conductivities instead of homogenous conductivities. Also we do not need to assume that the distance between electrode contacts are constant, another advantageous point, since it means that we can still use the data from laminar electrode even if one of the electrode contacts was malfunctioning [1]. In addition since the output of the iCSD method produces continuous CSD functions as output, we are able to use continuous filters such Gaussian filter to remove the noise, whereas for Standard CSD method we can only use three-point spatial filter, such as hamming filter.

For future studies, we can try to implement the other two types of the iCSD methods. We chose δ-source iCSD method because it was easier to implement and it needed the least numerical computations compare to the other two, but the limitations of this method compare to the other two is that it will give inaccurate estimates if the spacing between the electrodes are too large.

References

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