



## Computational Neuroscience

## Computationally efficient simulation of extracellular recordings with multielectrode arrays

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## HIGHLIGHTS

- ▶ We present a method that efficiently captures the spatial dependency of neural spikes.
- ▶ The information provided by compartment models is compressed and modeled.
- ▶ Efficient simulation of neural recordings with multielectrode arrays is facilitated.
- ▶ An object oriented simulation tool has been implemented.
- ▶ The method produces realistic test signals for validation of spike sorting methods.

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## ABSTRACT

In this paper we present a novel, computationally and memory efficient way of modeling the spatial dependency of measured spike waveforms in extracellular recordings of neuronal activity. We use compartment models to simulate action potentials in neurons and then apply linear source approximation to calculate the resulting extracellular spike waveform on a three dimensional grid of measurement points surrounding the neurons. We then apply traditional compression techniques and polynomial fitting to obtain a compact mathematical description of the spatial dependency of the spike waveform. We show how the compressed models can be used to efficiently calculate the spike waveform from a neuron in a large set of measurement points simultaneously and how the same procedure can be inverted to calculate the spike waveforms from a large set of neurons at a single electrode position. The compressed models have been implemented into an object oriented simulation tool that allows the simulation of multielectrode recordings that capture the variations in spike waveforms that are expected to arise between the different recording channels. The computational simplicity of our approach allows the simulation of a multi-channel recording of signals from large populations of neurons while simulating the activity of every neuron with a high level of detail. We have validated our compressed models against the original data obtained from the compartment models and we have shown, by example, how the simulation approach presented here can be used to quantify the performance in spike sorting as a function of electrode position.

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## 1. Introduction

Recently, there has been great interest in the development of brain–machine interfaces (BMIs) with the aim to control prosthetic devices, conduct basic research on the central nervous system (CNS) and to treat the symptoms of neurological disease. One way of performing signal acquisition in BMIs is to use chronically

implanted microelectrode arrays (Buzsáki, 2004) to measure the variation in extracellular potential resulting from discharges of action potentials in near by neurons. The extracellular representation of the action potential is usually referred to as a spike. Detecting spikes (Obeid and Wolf, 2004) in the extracellular signal and assigning them to their neurons of origin thus provides information about the activity patterns of individual neurons. The assignment part of that procedure is usually referred to as spike sorting (Lewicki, 1998). Since the performance in these processing steps is what determines the quality of the extracted information, the algorithms used for spike detection and spike sorting play a crucial role for the function of BMIs. Apart from the

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purely functional aspect, they are also important in the context of compressing the information contained in the neural signal for, e.g. wireless transmission and/or memory-efficient storage for off-line analysis.

The development of algorithms for information extraction is an important aspect of BMI development. During design and evaluation of such algorithms, test signals are needed with a priori known information content, in which the spike times of each individual neuron in the recording are known and can be compared with the output of the algorithms. In addition to having a priori known characteristics, the test signals need to have realistic signal properties and these properties need to be controllable to some extent. Realism is important for the future applicability of the results and controllability is important since it allows the algorithm designer to perform studies of algorithm performance in a wide range of scenarios that might be encountered in future applications.

The approaches to obtaining adequate test signals can be roughly divided into three categories, (1) simultaneous intra- and extracellular recordings, (2) purely synthetic recordings and (3) hybrid recordings. In simultaneous intra- and extracellular recordings, the intracellular membrane potentials of the cells of interest are measured directly and since the signal-to-noise ratio in these is normally high, they can be used as ground truth when assessing the performance in spike detection and sorting applied to the extracellular signal (Harris et al., 2000; Franke et al., 2010a). This class of test signals provides a high level of realism – the signals in question being real. However, they lack in some practical aspects since keeping track of all true neuronal activity is difficult or even impossible in many cases. Besides these practical problems, controllability of the recording properties is limited. Despite these downsides, simultaneous intra- and extracellular recordings could serve as ultimate benchmark signals in later steps of the algorithm design process.

Purely synthetic recordings are based on mathematical models of the signal generation process. The mathematical models can in turn be divided into two subcategories, (1) models based on compartment models of the neurons and (2) models based on fixed spike templates. Compartment models rely on more or less detailed models of the mechanisms involved in producing the action potential across the cell membrane and of the resulting signal measured outside the cell (Smith and Mtetwa, 2007; Gold et al., 2007; Pettersen and Einevoll, 2008). The extracellular signal is calculated by considering the voltage contribution of each point on each contributing neuron at each given time instance. The amount of details captured by such models thus leads to high computational demand, which makes them unpractical when modeling large populations of neurons. However, they are realistic in the sense that they do capture the variations in the spike waveform's shape that arise when placing the recording electrode in different measurement points (Gold et al., 2007). This feature is of great importance when modeling recording setups with multiple and/or positionally unstable recording electrodes, both of which are important factors to consider during development of algorithms for spike detection and spike sorting in realistic scenarios.

Models based on fixed spike templates assume that the extracellular spike waveform measured from a given cell can be selected from a library of spike templates and then scaled according to the cells distance from the electrode (Thorbergsson et al., 2009; Martinez et al., 2009). Apart from the amplitude scaling, template based models do not capture any spatial variations in the shape of measured spike waveforms. Therefore, despite their computational simplicity, they are not suitable for simulating recordings with multiple and/or positionally electrodes. A possible solution to this limitation is to first employ a compartment model to

calculate spike waveforms on a three dimensional grid of measurement points surrounding the neuron and then to interpolate the resulting waveforms to obtain waveforms in measurement points not lying on the simulation grid (Franke et al., 2010b). Despite the increased level of realism introduced with this approach, it requires extensive waveform interpolation and may therefore not be suitable for simulating very large populations of neurons.

In hybrid recordings, synthetic spike trains are overlaid on real recordings of background noise (Pouzat et al., 2002). They are thus advantageous in the sense that they have highly realistic signal properties, but lack in controllability for the same reasons as simultaneous intra- and extracellular recordings.

Considering the above, there is an obvious trade-off between realism and computational complexity when selecting among the available modeling approaches. Despite the ever increasing availability of computational resources that indeed contributes to minimizing the impact of this trade-off, we reason that computational efficiency should be striven for. General availability to fast and simple ways of modeling complex recording scenarios would be of great value to researchers during the development of algorithms for signal processing. The possibility of quickly generating test data to match a specific recording setup would speed up the development phase and save valuable time.

In this paper, we present a novel, computationally and memory efficient approach to generating test signals that combines the detail of compartment models with the computational simplicity of template based models. To achieve this combination, we applied traditional dimensionality reduction techniques and polynomial fitting to compress the description of the spatial dependency in spike waveforms provided by compartment models. We used the NEURON simulation environment (Hines and Carnevale, 1997) to simulate an action potential in a compartment model of a CA1 pyramidal neuron originally modeled in Gold et al. (2006) and used in Gold et al. (2007) and computed the extracellular spike waveforms on a three dimensional grid of measurement points using the line source approximation (LSA) (Holt and Koch, 1999). We then performed singular value decomposition (SVD) on the matrix containing the calculated spike waveforms and thereby obtained a set of basis waveforms describing the original spike matrix and their respective contributions to each of the original waveforms. Since most of the information describing the waveforms is contained in the first few (six) (Fee et al., 1996a; Thorbergsson et al., 2010) components of this decomposition, we achieved dimensionality reduction (compression) by discarding all other components. The result of this was a trivariate field of six dimensional vectors, whose elements described the basis waveform weights as functions of the measurement point coordinates relative to the neuron in question. To obtain a compact description of the spatial dependency of the basis waveform weights, we individually fit the elements of the weight vector field to polynomial functions of the measurement point coordinates. The modeling procedure was carried out for four different neuronal compartment models (cases A to D in Gold et al., 2007) and the parameters of the compressed models were optimized for each neuron to provide a good match between the spike waveforms provided by the NEURON simulations and our compressed models. The models were implemented into an object oriented simulation tool, written in *Matlab*, that facilitates fast and realistic simulations of multielectrode recordings with arbitrary geometries. Model validation was performed by comparing spikes from the original NEURON simulations with spikes generated by our models in terms of shape and amplitude, as well as by examination of synthetic signals in terms of noise properties. The applicability of our approach was evaluated in an example application by estimating the performance in spike sorting as a function of electrode position.

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