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Information extraction from biphasic concentration-response curves for data obtained from neuronal activity of networks cultivated on multielectrode-array-neurochips

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We aim to fit biphasic concentration-response curves to extract information about the effect of given biochemical substances to in-vitro neurons.

Neurons extracted from embryonic mice are cultivated on multielectrode-array-neurochips (MEA-neurochip) [1]. The activity of single neurons in such networks is recorded especially the change of network activity caused by long-term application of neuroactive substances. This results in quasi-stable patterns of neuronal activity. Based on the data, different features [2] are calculated adapted from spikes and bursts and separately displayed in concentration-response curves [3]. These concentration-response curves can exhibit non sigmoid shape, then indicating that different mechanisms affect the neuronal activity. Hence, the concentration-response curves presumably include currently hidden and unused information.

Methods
The concentration-response curve under consideration is given as mean spike rate depending on the logarithm of concentration. We present two methods to calculate biphasic concentration-response curves.

Firstly, a fitting algorithm, extending the method described in [3] is developed, leading not only to monophasic but also biphasic concentration-response curves. The fitting parameters gained with this method exhibit new features describing the effect of neuroactive substances in a new way.

Secondly, a smoothing spline [4] is applied to the data. Thereby efforts are being made to keep close at the data as well as to achieve a smooth curve. Computational Geometry is used to calculate the minimal and maximal curvature, the area under the curve as well as the local extrema of the fitted curve. These values quantify concentration dependent effects of the used substances.

We applied both approaches to datasets which are derived by adding agmatine or bicuculline, respectively, to the neuronal network (data by courtesy from Neuroproof GmbH). As these substances have biphasic or monophasic concentration-response curves, we were able to compare the values of the new features for these different effects.

Conclusion
The methods described above lead to new features describing the effect of increasing concentration on the mean spike rate of in-vitro neuronal networks. We aim to use these features for classification with machine learning algorithms like neuronal networks or support vector machines to identify unknown substances.

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