Simulation of Maturating Neuronal Networks derived from hPSCs*

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***Abstract*— In the past, we developed a simple model which simulates neuronal activity as observed in a neuronal network cultivated on a multielectrode array (MEA). The model is based on an inhomogeneous Poisson process to simulate neurons which are active without external input or stimulus as observed in MEA experiments. In the present work, the model is used to simulate a maturating neuronal cell network derived from human pluripotent stem cells (hPSCNN). These hPSCNNs exhibit highly variable network structure and time-varying dynamics. To explore and validate the developing burst and spike activities of such network simulations we applied spike train statistics. Calculated features adapted from spikes and bursts as well as the spike train statistics show that the presented model has potential to simulate maturating neuronal activity of hPSCNNs.**

I. INTRODUCTION

In the past, we built a model called INEX (INhibitory-EXcitatory) that was used to simulate neuronal activity recorded from frontal cortex tissue of embryonic mice using in vitro 2D microelectrode arrays (MEAs) (1). The aim of the presented work is the simulation of maturating neuronal cell networks derived from human pluripotent stem cells (hPSCNN).

II. METHODS

MEA recordings from hPSCNNs were done for approximately 300 seconds on the following measurement days: The first measurement day varied between 6 and 22 days of culturing in MEA. Thereafter, the developing networks were measured at 4-7 days after the first measurement, and the third measurement day was 2-4 days after the second measurement day. We will examine ten hPSCNN datasets with the mentioned characteristics.

The INEX model is based on an inhomogeneous Poisson process (2) to simulate neurons which are active without external input or stimulus as observed in MEA experiments. The four parameter types are chosen in such a way that the resulting spike trains resemble spike trains of 2D MEA experiments with hPSCNNs (3) with respect to spike and burst rate. A network with 1,000 neurons was simulated. The resulting spike train had a length of 300 seconds. We start with three percent of all possible connection which correspondence to the first measurement day. The connection probability will then increased to seven (second measurement day) and ten percent (third measurement day). The simulation tool was run with these constrains twenty times to get statistical significant data.

For validation, we calculated five features for each of the simulated spike trains using the burst analysis tool by Kapucu et al. (4) and compared them with the same features obtained from three MEA experiments with hPSCNNs.

III. RESULTS AND DISCUSSION

The experimental and modelled spike trains of the first measurement day showed just a few spikes. The number of spikes increases with the number of connections and by the second and third measurement day.

The simulated activity of the last measurement day exhibits typical spike and burst patterns as known from MEA experiments with (almost) maturated hPSCNNs (5). Partly synchronous spiking and bursting can be recorded for maturated hPSCNNs and can also been seen in the corresponding simulated spike trains. The variation of inhibitory and excitatory parameters were able to produce similar spiking characteristics as measured. The validation showed that all calculated averaged features of the INEX data are within the standard deviation of the MEA data.

IV. CONCLUSIONS

To conclude, the calculated features adapted from spikes and bursts as well as the spike train statistics show that the maturating process of hPSCNNs as observed in MEA experiments can be modeled by growing connectivity in the simulation network.

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