Stimulation effects on cortical culture development

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Introduction
We present continued work on long-duration, large-scale simulations of cortical culture development focusing on the effects of external stimuli on the growth process. Previous work showed that network behavior is dependent on scale (number of neurons) [1] and exhibits bifurcation behavior with only part of its parameter space corresponding to bursting as in the living preparation [2]. Preliminary results will be shown in which external input is presented during development and alters mature network behavior.

Methods
We constructed a model of development in cultures of dissociated cortical cells using a lumped, integrate-and-fire neuron model and dynamical synapses with activity-dependent facilitation and depression [3] and a model of activity-dependent connectivity development [4]. The simulated network included 10,000 neurons — excitatory, inhibitory, and spontaneously active — in a 100 × 100 rectangular array. The development rate constant was increased so the network would recapitulate its full, multi-week development over 60,000s (around 17h) of simulated time. Extensive tests were conducted to verify that this did not impact short-time-scale neuron firing behavior.

We utilized graphics processing unit (GPU) hardware and the compute unified device architecture (CUDA) API to yield an approximately 23x simulator speedup, allowing individual experiments to complete in 1–2 weeks on NVIDIA Tesla C1060 GPUs with 4 GB of memory or Tesla M2095 GPUs with 6 GB.

Application of external stimuli is being modeled by applying current pulses to 100 regularly-spaced neurons. Besides the no-input case, three stimulation patterns are being used: 1. completely synchronous pacemaker trains, 2. pacemaker trains with random cross-intervals between cells, and 3. Poisson trains for each cell with no inter-cell correlations.

Results
Figure 1 shows typical burst evolution in the absence of stimulation. This figure presents “mean burst” statistics plotted along simulation time (“Time”). The firing rate per neuron (“mean burst height”) as a function of time within each burst (“mean burst width”, up to 800ms in duration) was captured and averaged among all bursts within non-overlapping 1,000s windows. As can be seen, bursts began as quite broad (on the order of 1s), with low network firing rate; at steady state they were much sharper (around 200ms). This is consistent with in vitro experiments on dissociated rat cortex.

This bursting behavior emerges from network structure (balance of excitation and inhibition; connectivity patterns) and neurite outgrowth (extent of interconnectivity); it in turn affects structure and outgrowth during development. Depending on level of inhibition and neuron excitability, both inter-burst statistics (rate of burst production; regularity or irregularity of times of individual bursts) and intra-burst shape (burst intensity and duration) varied greatly or were even extinguished. This current work explores the effects of overall external input level, spatial patterns, and serial and spatial correlations.

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References