Research project agreement MSc Cognitive Neuroscience

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Specialization : Track 4: Brain Networks & Neuronal Communication

Number of ECs at time of signing of project agreement: 27

Number of ECs expected at start of research project: 48

(*note:* according to the EER, you need to have at least 42 EC to be able start your research project)

Information Research Institute & on-site supervisor

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Description of research project

Title of research project:
Distinct feedforward and feedback oscillatory interactions in a full-scale spiking network model

Provisional title of MSc thesis:
Distinct feedforward and feedback oscillatory interactions in a full-scale spiking network model

Author(s) of MSc thesis[1]:
D. Mingers

Start of research project:
15.02.2016

[1] Note that the MSc CNS student is always first author of his/her thesis and obligatory submission to the CNS Student Journal. However, the order of the authors should be reevaluated if a subsequent submission of the thesis to an external journal is considered.

Background of project:
Due to recent publications (e.g. Bastos et al., 2015; van Kerkoerle et al., 2014), I am interested in the effects of feedforward (FF) and feedback (FB) information processing along the visual pathway and the origins of oscillations representing these.

Specifically, I would like to study the interplay between single-neuron activation and inter-region connectivity in a computational model. The group of Markus Diesmann at Jülich Research Centre (JRC) has substantial experience in developing models that bridge these two scales and access to the computational power to run them. During my internship at the JRC, I would like to modify an extended version of the local microcircuit model (Potjans & Diesmann, 2014), that runs on the JUQUEEN supercomputer. The microcircuit model is designed as a full-scale model of ~10^5 neurons (sparsely connected, random balanced network, see Brunel, 2000; excitatory and inhibitory populations of LIF neurons for each of cortical layers 2/3, 4, 5, 6) that represent cortical microcircuits within macaque visual cortex. The model is built on experimental data to realistically represent anatomical and electrophysiological connectivity at the level of neural populations. In recent work, the microcircuit model has been extended to multiple areas (Schmidt et al., 2015; see Figure 1 for model summary). This multi-scale model will serve as the basis of the project at hand. While the model captures an asynchronous irregular ground state with reasonable firing rates and inter-area correlations, frequency-specific interactions such as alpha frequency coherence still need to be implemented.

Experimentally observed activity includes spontaneous synchronous firing behaviour at alpha frequency in L5 (Sun & Dan, 2009). One possible explanation for this specific frequency is the combination of neurons with different receptor types (Sun & Dan, 2009). It has been shown that isolated L5 with NMDA-driven cells, of which many are intrinsically rhythmic at 5-12 Hz, can express 4-7 Hz oscillations (Silva et al., 1991), which may contribute to alpha oscillations in vivo. Implementing NMDA-receptors that differ from AMPA-receptors in longer average time constants may thus help to obtain low-frequency activity. Experimental evidence further suggests that alpha oscillations are not expressed based on local spontaneous activity alone, but via cortico-thalamic feedback loops, primarily with the LGN and the pulvinar (Da Silva et al., 1980; Saalmann et al., 2012).

Van Kerkoerle et al. (2014) showed that alpha coherence provides FB and gamma coherence FF information streams. Bastos et al. (2015) similarly identified distinct frequency channels mediating FF and FB influences, with theta and gamma synchrony in the FF direction and betasynchrony in the FB direction. These distinct FF and FB interactions are further distinguished by their laminar profiles (van Kerkoerle et al., 2014), presumably related both to local laminar differences in the expression of oscillations at different frequencies (e.g. Sun and Dan, 2009) and to anatomical connectivity patterns between areas. For instance, FF connections preferentially arise from L2/3 and terminate in L4, whereas FB connections preferentially originate in infragranular layers and terminate outside L4 (Felleman and Van Essen, 1991; Markov et al., 2014). Another factor that may play a role in differential FF and FB interactions is the relative predominance of AMPA receptors associated with FF projections and NMDA receptors associated with FB projections (Self et al. 2012). The slow time course of NMDA activation may serve as a low-pass

filter to prevent high-frequency activity from being fed back from higher-order to lower-order areas (Jensen et al., 2015).

Aim of the project (be sure to include research question explicitly):
The activity observed within the local microcircuit model does not express all features as observed within the macaque. The aim of the project is to implement feedforward and feedback processes in the multi-area model (Schmidt et al., 2015) such that bottom-up processing is mediated by theta/gamma-frequency coherence between areas and, reversely, top-down processes by alpha/beta coherence. Furthermore, the layer specificity of these oscillatory interactions will be studied in terms of spiking and synaptic activity. The main question is which connection patterns, synaptic and intrinsic neuronal properties support the observed oscillatory interactions. For the explicit steps and associated sub-goals of the project, see the paragraph below.

Research plan (specifically indicate your role in the various phases of the project, i.e. design development, data acquisition, data analysis, reporting)
The project will have several stages, which advance until close-to-realistic coherence in respective layers and frequency bands between simulated populations can be observed:

1. Modeling of microcircuits for areas V1 and V2. Study of interactions between layers in both microcircuits, when forcing alpha synchrony in L5 of V2. This way, induce downstream alpha oscillations from L5.
2. For both microcircuits, implementation of subpopulations among excitatory neurons in L5: A fraction of pyramidals in L5 have inherent channel properties that make them resonate around alpha frequencies (Silva et al., 1991). Richardson et al. (2003) have shown that such neurons can be modelled as generalised IF neurons.
3. Implementation of synapses with longer time constants for FB connections from V2 to V1 to mimic NMDA kinetics (Self et al., 2012).
4. Once the above changes are implemented (and appropriately fine-tuned), differentiable feedforward and feedback processing can be expected. The model with areas V1 and V2 will then be extended to populations from 32 areas associated with visual processing at realistic connectivity, based on the work of Schmidt et al. (2015). This final step will use the JUQUEEN supercomputer.

After each step of simulation, the observed activity will be analysed with the measurements listed under “Methodology” (see below). See Potjans & Diesmann (2014) and Schmidt et al. (2015) for details regarding modeling. See Gewaltig & Diesmann (2007) for details regarding the NEST software. For the simulation at hand the SLI interface (an internal simulation language interpreter) of NEST will be used. All the above steps will be conducted by me. I will report and discuss my findings in weekly meetings with my supervisor. Interaction with members of the group of Moritz Helias (also at JRC) developing mean-field theory will provide hypotheses concerning origins of the observed oscillations and help with choosing appropriate parameter values.

Schedule (specifically state the <u>start and end dates</u> of the various phases of the research project and the writing of the thesis on a month-by-month basis)

Feb-Apr	Literature research, reviewing results of preliminary studies, familiarisation with software
May	Stage 1*
Jun	Stage 2*
Jul	Stage 3*
Aug	Stage 4*
Sep-Dec	Writing Thesis

*: Each stage includes theoretical parameter estimation, simulation, and evaluation (incl. hypothesis testing). Stages are based on the above paragraph.

Required methodology (data-analysis procedures, experimental techniques):
Simulation with NEST on a local high-performance cluster and the JUQUEEN supercomputer. Pre- and post-processing with Python to analyse and plot the oscillatory activity arising within the simulations. Coding will be based on the scripts of M. Schmidt and S. van Albada that were used in Schmidt et al. (2015). Data analysis will include spectral Granger causality, coherence, and Mutual Information of synaptic and spiking activity across areas. Inter-laminar, as well as inter-area propagation of activation will be analysed.

Construction of the model

A: Model summary	
Populations	254 populations: 32 areas with eight populations each (area TH: six)
Topology	—
Connectivity	area- and population-specific but otherwise random
Neuron model	leaky integrate-and-fire (LIF), fixed absolute refractory period (voltage clamp)
Synapse model	exponential postsynaptic currents
Plasticity	—
Input	independent homogeneous Poisson spike trains
Measurements	spiking activity, membrane potentials

B: Populations			
Type	**Elements**	**Number of populations**	**Population size**
Cortex	LIF neurons	32 areas with eight populations each (area TH: six), two per layer	N (area- and population-specific)

C: Connectivity	
Type	source and target neurons drawn randomly with replacement (allowing autapses and multapses) with area- and population-specific connection probabilities
Weights	fixed, drawn from normal distribution with mean w and standard deviation $\delta w = 0.1w$; 4E to 2/3E increased by factor 2 (cf. Potjans & Diesmann, 2014); weights of inhibitory connections increased by factor g; excitatory weights < 0 and inhibitory weights > 0 are redrawn
Delays	fixed, drawn from Gaussian distribution with mean d and standard deviation $\delta d = 0.5d$; delays of inhibitory connections factor 2 smaller; delays rounded to the nearest multiple of the simulation step size $h = 0.1\,\mathrm{ms}$, inter-areal delays derived from distances with constant transmission speed; delays $< 0.1\,\mathrm{ms}$ before rounding are redrawn

D: Neuron and synapse model	
Name	LIF neuron
Type	leaky integrate-and-fire, exponential synaptic current inputs
Subthreshold dynamics	$\frac{\mathrm{d}V}{\mathrm{d}t} = -\frac{V-E_\mathrm{L}}{\tau_\mathrm{m}} + \frac{I_\mathrm{s}(t)}{C_\mathrm{m}}$ if $(\mathrm{t} > \mathrm{t}^* + \tau_\mathrm{r})$ $V(t) = V_\mathrm{r}$ else $I_\mathrm{s}(t) = \sum_{i,k} w_k\, e^{-(t-t_i^k)/\tau_\mathrm{s}} \Theta(t - t_i^k)$ k: neuron index, i: spike index
Spiking	If $V(t-) < \theta \wedge V(t+) \geq \theta$ 1. set $t^* = t$, 2. emit spike with time stamp t^*

E: Input		
Type	**Target**	**Description**
Background	LIF neurons	independent Poisson spikes (see Table S1)

F: Measurements
Spiking activity and membrane potentials from a subset of neurons in each population

Table 1: Model description after Nordlie et al. (2009).

Table 1
Description of the construction of the multi-area model extracted from Schmidt et al., 2015. The construction of the microcircuit for each area is based on Potjans and Diesmann, 2012.

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Signatures

The signatories confirm the accuracy of all statements made on this form and agree to all principles and articles expresses as stated in the "MSc CNS Research Project Regulations". **Note**: there may be more than one on-site supervisor stated, but at least one of them must have a PhD.

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Educational supervisor *(if applicable)* Title + Name	Signature	Date
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