University of Sussex

School of Life Sciences

George Kemenes, PhD, DSc, FSB
Professor of Neuroscience
Director of Sussex Doctoral School

**Thesis reviewer's comments on the Doctoral Thesis "Regulation of cortical activity through inhibitory interneuron plasticity' by Karri Lämsä.**

Karri Lämsä's thesis has a very sound foundation in his impressive body of scientific work since the late 90's, the majority of which has been addressing the role of GABA and GABA-ergic interneurons in cortical network activity and in particular, synaptic plasticity. Many of his findings have been published in top-ranking journals, such as Science, Nature, Nature Neuroscience and Neuron. The highly professionally presented thesis uses his first-author Science (2007) and Nature Neuroscience (2005) papers and his more recent senior-author Journal of Neuroscience (2011), PLoS Biology (2016) and Brain Structure and Function (2017) studies as the basis for his application but also makes good use of information from his other highly-regarded work in this field.

The strength and novelty of the applicant's work lies in the fact that he and his colleagues have used a combination of state-of-the-art electrophysiological, neuroanatomical, cellular imaging and molecular methods, both in rodent and human cortical preparations, to demonstrate the key importance of long-term synaptic plasticity of the same common types of inhibitory interneurons in the regulation of cortical activity. Notably, they also have shown that the *in vitro* plasticity they described in acute brain slices can also be observed in the intact rodent brain *in vivo*. This lends very strong support to the notion that the synaptic plasticity mechanisms revealed by the *in vitro* protocols he and his colleagues used play an important role in learning.

The journals in which he has published his results use very rigorous reviewing criteria that ensures the validity of the data presented in the papers and the thesis itself. But as a neuroscientist also using the same combination of methods in my research that the applicant and his colleagues have used to make their significant discoveries, I am also in a position to confirm that all the work presented in the thesis and published by the applicant conforms to the highest standards of scientific investigations used in the field.

I therefore also confirm that all the theses presented in detail by the applicant can be accepted as new scientific discoveries in the field of mammalian, including human, cortical plasticity.

contact us

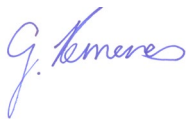
**George Kemenes, PhD, DSc**
Professor of Neuroscience

School of Life Sciences
John Maynard Smith Building
University of Sussex, Brighton
BN1 9QG United Kingdom

**T** +44(0) 1273 872762
**M** +44(0) 7780662319
**F** +44(0) 1273 678535
G.Kemenes@sussex.ac.uk
www.sussex.ac.uk

The main criticism I have regarding the thesis and the applicant's published work in general is the apparent lack of discussion of the potentially evolutionarily conserved role of inhibitory interneurons in the regulation of neuronal network activity, including circuit plasticity – and not just between the rodent and human brain. There are numerous examples of studies from both invertebrate and lower vertebrate model systems pre-dating or contemporary to the applicant's work where the roles of inhibitory neurons have been elucidated in the regulation of network activity, such as central pattern generation or indeed network and behavioural plasticity, and yet there is no reference to these in the thesis, or as far as I can see, in the applicant's published work. I would have welcomed a brief discussion of the broader evolutionary context of the importance of inhibitory interneuronal activity/plasticity to be included in a Doctoral Thesis and also in the original work underpinning it and was somewhat disappointed not to find it there. I am a neuroscientist working with an invertebrate model system and when we publish our findings we always put them into the context of relevant findings in other invertebrate as well as vertebrate model systems; it would be nice if this were reciprocated by neuroscientists using vertebrate models.

Another area that the applicant could have addressed in a bit more detail in the discussion section of the thesis is how long-term synaptic and non-synaptic (intrinsic) plasticity may work together to result in network and behavioural level plastic changes. It is now well documented in both vertebrates and invertebrates that non-synaptic as well as synaptic plasticity can be a substrate for long-term memory and in the thesis the applicant does refer to the fact that GABAergic neurons undergo a wide range of synaptic and non-synaptic activity-induced plasticity processes. It would have been helpful if the thesis had explained briefly what the main findings were of the studies where both types of plasticity were investigated in the same neurons.



Professor George Kemenes

26 November 2019