Neuronal oscillations as a critical phenomenon and its implications for information processing

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Summary

Information processing in the brain happens at multiple levels, from integrating information at the single neuron level, to communication between neurons and neuronal networks at different spatial and temporal scales. Neuronal oscillations and, more recently, neuronal avalanches have been proposed to play an important role in this communication. Interestingly, both oscillations and neuronal avalanches exhibit scale-free dynamics, a hallmark of critical behavior. Empirical studies have shown that scale-free modulation of oscillations can predict behavioral variability in humans, and is altered in epilepsy, schizophrenia and Alzheimer's disease. Theoretical studies have linked criticality in terms of neuronal avalanches to desired information-processing characteristics such as reactivity, adaptability and robustness to input, and the activation of neuronal representations in the form of meta-stable activity patterns. This led to the questions of whether these different forms of critical-state dynamics are related, and what is the functionality of critical oscillations?

The major aim of this thesis was to understand the mechanism and information processing functionality of scale-free amplitude modulation of oscillations. To accomplish this I created a neuronal network model where scale-free oscillations emerged through the mechanism of balanced excitatory and inhibitory connectivity. I found that networks poised at this balanced state also showed scale-free spreading of activity in the form of neuronal avalanches. By integrating the previously separate fields of neuronal avalanches and oscillations into a new form of network dynamics, multi-level criticality, it raised the possibility that modulations in oscillations may be used as a proxy to predict changes in the neuronal criticality and excitation-inhibition ratio of a network. It also allowed me to investigate the implications of critical oscillations for information processing in neuronal networks.

To understand how critical oscillations affect neuronal network function I stimulated networks which possessed sub-, critical and super-critical dynamics. I found that state-dependent information processing capabilities that had been previously linked to

neuronal oscillations only occurred close to the critical state. In other words, to understand the momentary reactivity of a network, insight into the dynamic state over long time periods is needed, which can be detected by the proximity of the oscillatory dynamics to the critical state. This finding has wide-ranging implications for understanding and detecting behavioral variability, and loss of function, in healthy and diseased neuronal networks.

Biomarkers of disordered neuronal networks are essential for the detection and treatment of disease. Imbalances in the excitation-inhibition ratio (E/I) at the cellular and network level have emerged as a potential biomarker of multiple disorders including autism and schizophrenia. However, it has remained difficult to define E/I at the neuronal network level and detect it using non-invasive recordings in humans. Using the framework of critical-state dynamics and the model of critical oscillations that I had developed, I investigated whether it was possible to estimate E/I ratio from neuronal network oscillations. This led to a new biomarker, $\widehat{\mathrm{E/I}}$, that could be applied to magneto- and electroencephalography (M/EEG) recordings. Applying this new biomarker to human subjects performing a threshold stimulus detection task, we found that $\widehat{\mathrm{E/I}}$ during the task varied between subjects, and that these differences could explain the neuronal network response to the stimulus. This biomarker has great potential for detecting imbalances in E/I, which would be useful for disordered networks and their response to treatment.

Overall, in this thesis, I show that scale-free neuronal oscillations can be understood through the framework of criticality, and that by creating a neuronal network to model them it is now possible to understand the effects of these dynamics on the information processing capabilities of neuronal networks. This will allow for a greater understanding of how and why the dynamics of neuronal oscillations are altered in healthy and diseased networks.

Samenvatting

Informatieverwerking in de hersenen vindt plaats op verschillende niveaus, van het integreren van informatie door individuele neuronen, tot communicatie tussen neuronen en hersengebieden op verschillende spatiële en temporele schalen. Neuronale oscillaties en, meer recentelijk, cascades van neuronale activiteit ('lawines') worden verondersteld een belangrijke rol te spelen in deze communicatie. Interessant is dat zowel oscillaties als neuronale lawines schaalvrije dynamiek vertonen; een kenmerk van kritisch gedrag. Empirisch onderzoek heeft aangetoond dat schaalvrije modulatie van oscillaties variatie in menselijk gedrag kan voorspellen en afwijkt bij epilepsie, schizofrenie en de ziekte van Alzheimer. Theoretisch onderzoek heeft kritisch gedrag in de vorm van neuronale lawines in verband gebracht met wenselijke kenmerken van informatieverwerking zoals reactiviteit, aanpassingsvermogen, robuustheid ten opzichte van de input en de activatie van neuronale representaties in de vorm van meta-stabiele activiteitspatronen. Dit heeft geleid tot de vraag of er een relatie is tussen deze verschillende vormen van kritisch gedrag (*critical-state dynamics*), en wat de functie is van kritische oscillaties.

Het belangrijkste doel van dit proefschrift was om inzicht te krijgen in het mechanisme en de functionaliteit van schaalvrije amplitudemodulatie van oscillaties. Om dit te bereiken heb ik een neuronaal netwerkmodel ontwikkeld waarin schaalvrije oscillaties voortkwamen uit het mechanisme van gebalanceerde exciterende en inhiberende verbindingen. Ik constateerde dat netwerken die in deze gebalanceerde toestand verkeerden ook schaalvrije spreiding van activiteit vertoonden in de vorm van neuronale lawines. Door het samenbrengen van de voorheen gescheiden onderzoeks gebieden van neuronale lawines en oscillaties in een nieuw soort netwerkdynamica, 'multi-level criticality', kwam de mogelijkheid naar voren dat modulaties in oscillaties gebruikt kunnen worden als maatstaf van kritisch neuronale dynamiek en de balans tussen excitatie en inhibitie van een netwerk. Daarnaast maakte het mogelijk om de implicaties van kritische oscillaties voor de informatieverwerking in neuronale netwerken te onderzoeken.

Om inzicht te krijgen in de invloed van kritische oscillaties op de werking van neuronale netwerken heb ik netwerken gestimuleerd die sub-, kritisch en superkritische dynamiek vertoonden. Ik constateerde dat toestandsafhankelijke informatieverwerkingscapaciteiten die voorheen in verband werden gebracht met neuronale oscillaties alléén dicht bij de kritische toestand voorkwamen. In andere woorden, om de reactiviteit van een netwerk op een willekeurig moment te kunnen begrijpen, is inzicht vereist in de dynamische toestand over langere tijdsperiodes, die gerelateerd kan worden aan hoe dicht bij de kritische toestand de oscillatiedynamiek zich bevindt. Dit resultaat heeft verstrekkende implicaties voor het inzicht in gedragsvariatie en functieverlies in gezonde en zieke neuronale netwerken.

Biomarkers van de toestand van neuronale netwerken zijn essentieel voor de opsporing en behandeling van ziektes. Onevenwichtigheden in de excitatie/inhibitieratio (E/I) op cellulair en netwerkniveau zijn naar boven gekomen als een potentiële biomarker voor verschillende stoornissen, waaronder autisme en schizofrenie. Echter, het is nog altijd moeilijk om E/I te definiëren op neuronaal netwerkniveau, en om het door non-invasieve metingen in mensen in te schatten. Met gebruik van het raamwerk van kritische toestandsdynamiek en het model van kritische oscillaties dat ik heb ontwikkeld, heb ik onderzocht of het mogelijk is om de E/I ratio te schatten aan de hand van neuronale netwerkoscillaties. Dit heeft geleid tot een nieuwe biomarker, $\widehat{E/I}$, die zou kunnen worden toegepast op magneto- en elektro-encefalografie (MEG/EEG) opnames. Het toepassen van deze nieuwe biomarker bij proefpersonen die zwakke prikkels moesten detecteren, bracht aan het licht dat $\widehat{E/I}$ tijdens de taak verschilt per proefpersoon, en dat deze verschillen de reactie van het neuronale netwerk op de prikkel konden verklaren. Deze biomarker heeft een groot potentieel voor het detecteren van onevenwichtigheden in E/I, wat bruikbaar zou kunnen zijn bij het detecteren van door ziekte aangetaste netwerken en hun reactie op behandeling.

Al met al laat ik in dit proefschrift zien dat schaalvrije neuronale oscillaties kunnen worden begrepen middels het *criticality* raamwerk, en dat met de ontwikkeling van een neuronaal netwerk dat ze modelleert het nu mogelijk is om de effecten van dit gedrag op de informatieverwerkingscapaciteiten van neuronale netwerken te begrijpen. Dit kan bijdragen aan een groter inzicht in hoe en waarom de dynamiek van neuronale oscillaties verschilt in zowel gezondheid en ziekte.

Samenvatting

Publications

Detrended fluctuation analysis: A scale-free view on neuronal oscillations
Richard Hardstone, Simon-Shlomo Poil, Giuseppina Schiavone, Rick Jansen, Vadim V Nikulin, Huibert D Mansvelder, Klaus Linkenkaer-Hansen
Published in Frontiers in Physiology Volume32 (2013)

Critical-State dynamics of avalanches and oscillations jointly emerge from balanced excitation/inhibition in neuronal networks
Simon-Shlomo Poil*, Richard Hardstone*, Huibert D Mansvelder, Klaus Linkenkaer-Hansen *(Joint first Author*)*
Published in Journal of Neuroscience Volume 32 /Issue 29 (2012)

Versatility of neuronal networks is maximized in the critical state
Richard Hardstone, Jan-Matthis Lueckmann, Jan Bim, Huibert D. Mansvelder, Klaus Linkenkaer-Hansen
In preparation

Cortical excitation-inhibition ratio explains individual variation in perceptual processing
Richard Hardstone, Jan-Matthis Lueckmann, Jonni Hirvonen, Satu Palva, Huibert D. Mansvelder, J. Matias Palva, Klaus Linkenkaer-Hansen
In preparation

Publications not included in thesis:

The Amsterdam Resting-State Questionnaire reveals multiple phenotypes of resting-state cognition
B Alexander Diaz, Sophie Van Der Sluis, Sarah Moens, Jeroen S Benjamins, Filippo Migliorati, Diederick Stoffers, Anouk Den Braber, Simon-Shlomo Poil, Richard Hardstone, Dennis Van't Ent, Dorret I Boomsma, Eco De Geus, Huibert D Mansvelder, Eus JW Van Someren, Klaus Linkenkaer-Hansen
Published in Frontiers in Human Neuroscience, vol. 7 2013

The ARSQ 2.0 reveals age and personality effects on mind-wandering experiences
B Alexander Diaz, Sophie Van Der Sluis, Jeroen S Benjamins, Diederick Stoffers, Richard Hardstone, Huibert D Mansvelder, Eus JW Van Someren, Klaus Linkenkaer-Hansen
Published in Frontiers in Psychology, vol. 5 2014

The Neuronal Network Oscillation as a Critical Phenomenon
Richard Hardstone, Huibert D Mansvelder, Klaus Linkenkaer-Hansen
Book chapter – Criticality in Neural Systems, Wiley-VCH Verlag GmbH & Co. KGaA 2014

Resting-state cognition and EEG biomarkers are associated with and predict sleep-onset latency

B. Alexander Diaz, Richard Hardstone, Eus J.W. van Someren, Huibert D. Mansvelder and Klaus Linkenkaer-Hansen

In revision in Frontiers in Human Neuroscience

Curriculum Vitae

Richard Hardstone was born on 16th December 1982 in Margate, United Kingdom. From 2002-2006 he studied computing at Imperial College London, and wrote his master's thesis on a new method to predict the behaviour of groups of robots that acted according to swarm intelligence. He moved to the Netherlands in 2007 to study media technology at Leiden University which included taking the neuroinformatics course at VU Amsterdam. The neuroinformatics course led to an internship project, focussed on a model of the dynamics of neuronal oscillations, in the group of Klaus Linkenkaer-Hansen in September 2009. This led to funding from the Neuroscience Campus Amsterdam (March 2010) and Netherlands Organization for Scientific Research (NWO) (March 2012) to complete the PhD. Since leaving the Netherlands in 2015 he has been working as a post-doc in the group of Biyu He, at the National Institute of Health in Bethesda,USA. The group will be moving to the Neuroscience Institute at New York University Medical School in 2016.

Curriculum Vitae

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Huib for creating a great department to work in, and providing financial support to give me time to find funding to finish my phd. Hugely knowledgeable about all areas of neuroscience, he has a great ability to get to the heart of the problem and showed me that modelling succeeds most when it does more than reproduce data, and actually produces knowledge and hypotheses that can inform and guide experiments.

Throughout my PhD I worked with many bachelors and masters internship students, who produced a great amount and quality of work and allowed the projects to move in different directions. For the modelling work, Jan Bim, Jan-Matthis, Istvan and Arthur used their excellent programming skills to make much progress in understanding how critical oscillations occur and what their function is. This was a tough and often frustrating task, and you all provided innovative ways of approaching the problems set. The sleep biofeedback project, worked on by Thijs, Michele, Kim, Natalie and Lorena, was a lot of fun and also a lot of hard work during the hours of testing and recordings that were put in, and I am still hopeful that the method will one day be able to help people with insomnia. I am really happy that so many of you have continued as researchers, and I wish you all the best in the future, and that we work together again someday.

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To my officemates over the years (Lawrence, Andy, Johannes, Ioannis, Pieter-Laurens, Martina, Julia, Tim, Roel, Hemanth, Keerthi, Chris) thanks for putting up with me and my erratic working habits, playing the *occasional* game of table tennis, and surviving the extreme temperatures that our office seemed to provide. To the rest of INF (Rhi, Chris, Tim, Tjeerd, Natalia, Bernard, Marta, Maria, Adrian, Jaap and many more…) thanks for all the great outings and managing to stay awake during my presentations.

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