Variability and compensation in Alzheimer's disease across different neuronal network scales

Claudia Bachmann
Variability and compensation in Alzheimer’s disease across different neuronal network scales

Claudia Bachmann
Contents

Abstract

Überblick

Declaration of contributions

Acknowledgements

1 Introduction

1.1 Alzheimer’s disease - a disease with many facets

1.2 The concept of homeostasis in biology exemplified by neuronal network dynamics

1.3 Homeostasis in neuronal networks suffering Alzheimer’s disease

1.4 Methodological considerations

1.4.1 What does fMRI measure?

1.4.2 Introduction into graph theory

1.4.3 Network simulation and performance measures

1.5 Dealing with Alzheimer’s disease and its effects on homeostatic regulation

2 Inferring health conditions from fMRI-graphs

2.1 Introduction
2.2 Results ................................................................. 28
  2.2.1 Selection of clinical use case and fMRI-data acquisition .......... 28
  2.2.2 Calculation of probabilities: exchangeability ................... 29
  2.2.3 Trimming the data space: functional connectivity ............... 32
  2.2.4 Trimming the distribution space: models by sufficiency and generalized normals ..................................................... 34
    2.2.4.1 Parametric models ........................................... 34
    2.2.4.2 Models by sufficient statistics .............................. 35
    2.2.4.3 Edgeworth’s “method of translation”: generalized normal models .......................................................... 36
    2.2.4.4 Generalized normal models in our study .................... 39
  2.2.5 Model comparison and selection ..................................... 41
    2.2.5.1 Criteria for model comparison ............................... 41
    2.2.5.2 Results for our three models ............................... 44
    2.2.5.3 Contrast with other model-comparison criteria ............. 45
    2.2.5.4 Final assessment of models ................................. 47
2.3 Discussion ........................................................... 49
  2.3.1 Summary ......................................................... 49
  2.3.2 Comparison with other studies and methods ..................... 50
  2.3.3 Possible improvements ........................................ 51
2.4 Methods .............................................................. 52
  2.4.1 Data preprocessing .............................................. 52
  2.4.2 The normal model with conjugate prior ........................ 53
  2.4.3 Decision theory and utility .................................... 54
3 Extraction and analysis of graphs from rfMRI as diagnostic tool for AD 57

3.1 Introduction ................................................................. 58

3.2 Results ................................................................. 62

3.2.1 Graph construction .................................................. 62

3.2.1.1 Vertex definition by means of clustering ................. 62

3.2.1.2 Edge definition by means of functional connectivity .... 64

3.2.2 Graph properties .................................................. 66

3.2.3 Evaluation of graph construction methods based on negative surprise 70

3.3 Discussion ............................................................. 74

3.4 Methods ................................................................. 83

3.4.1 Data acquisition .................................................... 83

3.4.2 Preprocessing of fMRI-data and extraction of cortical data .... 84

3.4.3 Data-driven and Atlas based clustering of cortical voxels .... 84

3.4.3.1 Atlas-based clustering ....................................... 85

3.4.3.2 Ward clustering ............................................... 85

3.4.3.3 Region growing and selection ............................. 85

3.4.4 Edge definition .................................................... 87

3.4.5 Graph properties ................................................ 89

3.4.6 Statistical model ................................................ 92

3.4.7 Supportive evaluation measures of graph construction methods .... 93

3.4.7.1 Significance test ........................................... 93

3.4.7.2 Dendrograms of subject order ............................ 93

3.4.7.3 Support vector machines .................................. 94

3.5 Supplementary Tables and Figures .................................. 94
4 Firing rate homeostasis counteracts synapse loss

4.1 Introduction ....................................................... 97

4.2 Results ........................................................... 100

4.2.1 Computational network model of Alzheimer’s disease .......... 100

4.2.2 Total synaptic contact area and firing statistics ................. 103

4.2.3 Perturbation sensitivity and linear stability .................... 104

4.3 Discussion ....................................................... 109

4.4 Methods .......................................................... 115

4.4.1 Network model ................................................. 115

4.4.2 Synaptic contact area and characterization of network activity ... 116

4.4.3 Linearized network dynamics and stability analysis ............ 117

4.5 Supplementary Materials ...................................... 123

4.5.1 Network model ................................................. 123

4.5.2 Lists of parameters ............................................ 124

4.5.3 Canceling of the synaptic-weight variance by the input variance ... 126

4.5.4 Unspecific synapse loss and homeostasis ....................... 126

5 Discussion ......................................................... 129

5.1 Summary of the results ........................................... 129

5.2 The reciprocal interactions of different brain scales in Alzheimer’s disease ... 131

5.3 Outlook ........................................................... 133

Bibliography ......................................................... 137
Variability and compensation in Alzheimer’s disease across different neuronal network scales

Claudia Bachmann