Multimodal Analysis of Directional Interactions in Oscillatory Networks of the Brain

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Abdul Rauf Anwar

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1. Berichterstatter:	Prof. Dr.-Ing. Ulrich Heute
2. Berichterstatter:	Prof. Dr. med. Günther Deuschl
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Abdul Rauf Anwar

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Declaration

This thesis is an account of research undertaken between February 2011 and July 2014 at the Department of Digital Signal Processing and System Theory, Institute of Electrical and Information Technology, Faculty of Engineering, University of Kiel, Kiel, Germany.

Except where acknowledged in the customary manner, the material presented in this thesis is, to the best of my knowledge, original and has not been submitted in whole or part for a degree in any university. This work was prepared to be in compliance with the rules set by the German Research Foundation (Deutsche Forschungs Gemeinschaft, DFG).

Abdul Rauf Anwar
Kiel, July 2014

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Abstract

The functional working of the brain is not dependent on its structural anatomy, i.e, in order to carry out a neurologically-demanding task, different structurally remote regions of the brain work synchronously with each other. The analysis of functional connectivity of the brain is not straight forward. Combination of different modalities simultaneously to record brain activity can be helpful in explaining the functional networks involved during certain tasks. Different modalities capture different dynamics of cortical activity, for example, electroencephalography, magnetoecephalography, and near-infra red spectroscopy offer a very good temporal resolution, while the functional magnetic-imaging signal has a fine spatial resolution. The concept of causality can help, indirectly, to determine the chronological order of the signals flowing in the brain. It states that by determining the direction of information flow between two signals, we can find out which of the two signals started farther back in time, and hence, comes from the source. Moreover, the conventional methods of understanding the relationship between two signals, like correlation, are unable to tell us anything about the causality.

The causality can be estimated in time-domain, by using methods like conditional Granger causality, which compares variances of different models. Furthermore, frequency-domain causality methods are an indispensable tool when the aim is to estimate causality between neuronal oscillations of a particular frequency. Methods like partial directed coherence and re-normalized partial directed coherence are some of the important frequency-domain causality measures. By using a combination of Kalman filters, we can develop methods like time-resolved partial directed coherence, which not only looks at the causality at a certain frequency, but can also reveal the time-dynamics of estimated causality. In this thesis, all of the aforementioned causality measures were applied on model data to corroborate them, and furthermore, on actual medical data to examine various oscillatory functional networks.

Along with the investigation of different oscillatory networks in the brain, structural connectivity within the brain, using the white matter tracts, was also analyzed using graph-analysis algorithms. Comparing network measures of the brain of Parkinsonian patients and those of healthy subjects can reveal the structural differences between the two groups. Moreover, a method based on the statistical properties of the individual neurons is also proposed for the optimum postoperative stimulation contact for the deep-brain stimulation.

Zusammenfassung

Die funktionale Arbeitsweise des Gehirns ist nicht abhängig von seiner strukturellen Anatomie; das heißt, für die Durchführung einer neurologisch anspruchsvollen Aufgabe arbeiten verschiedene strukturell entfernte Regionen des Gehirns synchron miteinander. Die Analyse der funktionellen Konnektivität des Gehirns ist nicht trivial. Die Erfassung der Gehirnaktivität durch verschiedene Modalitäten kann gleichzeitig zur Erklärung der funktionellen Netzwerke für bestimmte Aufgaben sehr hilfreich sein. Unterschiedliche Modalitäten erfassen unterschiedliche Dynamiken der kortikalen Aktivität; zum Beispiel bietet Elektroenzephalographie eine sehr gute zeitliche Auflösung, während die funktionelle Magnetresonanztomographie eine feine räumliche Auflösung hat. Der Begriff der Kausalität kann indirekt helfen, die Reihenfolge zwischen zwei Signalen im Gehirn zu bestimmen. Das besagt, dass wir durch die Bestimmung der Richtung des Informationsflusses zwischen zwei Signalen herausfinden können, welches der beiden Signale in der Zeit eher begonnen hat und damit die Quelle darstellt.
Die Kausalität kann im Zeitbereich mit Methoden wie bedingte Granger-Kausalität abgeschätzt werden, die die Abweichungen zwischen verschiedenen Modellen vergleicht. Außerdem sind Frequenzbereichs-Kausalitäts-Methoden ein unverzichtbares Werkzeug, wenn es das Ziel ist, die Kausalität zwischen neuronalen Oszillationen bestimmter Frequenzen zu schätzen. Methoden wie *partial directed coherence* und *re-normalized partial directed coherence* sind einige der wichtigen Frequenzbereichs-Kausalitäts-Messungen. Durch die Verwendung einer Kombination von Kalman-Filtern können Methoden wie die *time-resolved partial directed coherence* entwickelt werden, die nicht nur die Kausalität im Frequenzbereich, sondern auch die Zeit-Dynamik der geschätzten Kausalität zeigen kann. In dieser Arbeit wurden alle oben genannten Messtechniken auf Modell-Daten angewendet, um sie zu untermauern, und darüber hinaus auf verschiedene funktionale Oszillations-Netzwerke.
Zusammen mit der Untersuchung verschiedener Schwingungs-Netzwerke im Gehirn wurde strukturelle Konnektivität im Gehirn mit Hilfe der weißen Substanz ebenfalls mit Grafik-Analyse-Algorithmen analysiert. Die Netzwerk-Messung im Gehirn bei Parkinson-Patienten und gesunden Probanden kann die strukturellen Unterschiede zwischen den beiden Gruppen schätzen. Darüber hinaus wird ein Verfahren auf der Basis der statistischen Eigenschaften der einzelnen Neuronen auch für die optimalen Bestimmungen des postoperativen Stimulationskontaktes für die tiefe Hirnstimulation vorgeschlagen.

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Abbreviations

A/D	Analog to digital
AAR	Adaptive auto-regression
ADF	Augmented Dickey-Fuller
AIC	Akaike information criterion
AR	Auto-regressive
ARIMA	Auto-regressive Integrated Moving-average
ARMA	Auto-regressive Moving-average
BA	Background activity
BIC	Bayesian information criterion
BOLD	Blood oxygen level dependent
BS	Brainstem
C	Central
CAT	Criterion auto-regressive transfer function
CBSE	Classification-based signal enhancement
CER	Cerebellum
CFS	Complex finger sequence
CGC	Conditional Granger causality
CMC	Contralateral motor cortex
DBS	Deep brain stimulation
DC	Directed coherence
dDTF	Direct Directed transfer function
DEKF	Dual extended Kalman filter
DF	Dickey-Fuller
DICS	Dynamic imaging of coherence sources
DMN	Default-mode network
DPARSFA	Data pre-processing assistant for resting state fMRI advanced
DTF	Directed transfer function
DTI	Diffusion tensor imaging
EC	Eyes close
EEG	Electroencephalography
EKF	Extended Kalman filter

EMD	Empirical mode decomposition
EMG	Electromyography
EO	Eyes open
ET	Essential tremor
F	Frontal
FA	Fractional anisotropy
fMRI	Functional magnetic resonance imaging
FPE	Final predictoin error
FR	Firing rate
FT	Finger tapping
FWHM	Full with at half maximum
GDP	Gross domestic product
gPDC	Generalized partial directed coherence
Gpi	Globus pallidus
HR	Hemodynamic response
HRF	Hemodynamic response function
KF	Kalman filter
KPSS	Kwiatkowski-Phillips-Schmidt-Shin
KS	Kolmogrove-Smirnov
LFF	Low-frequency fluctuations
MA	Moving-average
MEG	Magnetoencephalogrpahy
MER	Micro-electrodes recording
ML	Maximum likelihood
MNI	Montreal neurological institute
MRI	Magnetic resonance imaging
MVAR	Multivariate auto-regressive
NIRS	Near-infra-red spectroscopy
O	Occipital
P	Parietal
PC	Personal computer
PD	Parkinson's disease
PDC	Partial directed coherence
PFC	Prefrontal cortex
PGC	Partial Granger causality
PMC	Premotor cortex
PPN	Pedunculopontine nucleus
PSD	Power spectral density
RA	Relative anisotropy
RIS	Rissanen's minimum description-length

ROI	Region of interest
rPDC	Re-normalized partial directed coherence
RSN	Resting state network
SFS	Simple finger sequence
SIFT	Source information flow toolbox
SMA	Supplementary motor area
SMC	Sensory motor cortex
SNR	Signal-to-noise ratio
SNr	Substantia nigra
SQUID	Superconducting
SS	State-space
STN	Subthalamic nucleus
T	Temporal
TE	Echo time
tPDC	Time-resolved partial directed coherence
TPN	Task-positive network
TR	Repetition time
VIM	Ventrointermediate nucleus
VR	Volume ratio

Notation

Functions and Operators

AR(p)	Auto-regressive model with order p
ARIMA(p,d,q)	Auto-regressive integrated moving average model with order p,d, and q
ARMA(p,q)	Auto-regressive moving average model with order p and q
A^{T}	Transpose of matrix $\mathbf{A}$
$\lvert\mathrm{A}\rvert$	Determinant of matrix $\mathbf{A}$
a^{*}	Conjugate of a
$\lvert\mathrm{a}\rvert$	Absolute of a
E.	Expectation operator
$\mathcal{F}(.)$	Fourier transformation
MA(q)	Moving average model with order q
$\bar{\mathrm{x}}$	Mean of signal x
$\hat{\mathrm{x}}$	Estimate of signal x
$\hat{\mathrm{x}}^{-}$	A priori estimate of signal x

List of Variables

a_{ij}	MVAR coefficient of causality
$a_{ij}(r)$	Time-varying MVAR coefficient of causality
$\mathbf{A}$	System matrix
$A_{ij}(\omega)$	Element of Fourier-transformed MVAR coefficient matrix
$\mathbf{A}(\omega)$	Fourier-transformed MVAR coefficient matrix
$\mathbf{A}_{k-1}$	Partial derivative of transition matrix
ASP	Average shortest path
AC	Assortativity coefficient
$\mathbf{B}$	Input matrix
c_{ij}	Auto-covariance function according to least square estimation
C_{xy}	Coherence between signal x and y
$Cov(xy)$	Covariance between signal x and y

$\mathbf{C}$	Output matrix
$\mathbf{C}_k^w$	Partial derivative of innovation noise
C_i	Local clustering coefficient
CPL	Characteristic path length
C_g	Global clustering efficiency
d_{ij}	Shortest path length
$\mathbf{D}$	Feed-through matrix
$\hat{e}_{fo}$	Estimate of forward prediction error
$\hat{e}_{bo}$	Estimate of backward prediction error
$\mathbf{E}(z)$	Z-transformation of noise vector
E_g	Global efficiency
$\mathbf{f}(k,\mathbf{x}_k)$	Non-linear transition matrix
$\mathbf{F}_{jj}$	Element of inverse of signal covariance matrix
$\mathbf{F}_{k+1}$	Transition matrix
$\mathcal{F}_{y\to x}$	Granger causality from signal y to signal x
$\mathcal{F}_{y\to x\|z}$	Conditional Granger causality from signal y to signal x
$g_{i\longleftrightarrow j}$	Shortest path
$gPDC_{ij}(\omega)$	Generalized partial directed coherence
G_k	Kalman gain
h_{ij}	Connection status
$\mathbf{h}(k,\mathbf{x}_k)$	Non-linear measurement matrix
$\mathbf{H}_k$	Measurement matrix
$\mathbf{H}(e^{j\omega})$	Transfer function matrix
$H_{ij}(e^{j\omega})$	Element of transfer function matrix
$\mathbf{I}$	Identity matrix
$\mathbf{Inf}_k$	Vector with state and signal information available till point k
k_i	Number of neighbors of a node
$\hat{k}_p$	Reflection coefficient
$\mathbf{K}_k^x$	Kalman gain for state estimation
$\mathbf{K}_k^w$	Kalman gain for weight estimation
$p(k^{'})$	Probability of a node having degree $k^{'}$
$\mathbf{p}_{w_0}$	Initial weight error covariance matrix
$\mathbf{p}_{x_0}$	Initial state error covariance matrix
$P_{ij}(\omega)$	Partial coherence between signal x_j and x_i
$\mathbf{Q}_k$	Variance of process noise
Q_m	Modularity
$rPDC_{ij}(\omega)$	Re-normalized partial directed coherence
$\mathbf{R}_k$	Variance of measurement noise
R_{xy}	Correlation vector between signal x and y
$\hat{R}_x$	Auto-covariance function according to Yule-Walker estimation

$\mathbf{R}(k,l)$	Signal covariance matrix
$\mathbf{R}^r$	Innovation covariance matrix in DEKF estimation
$\mathbf{R}^v$	Process noise covariance matrix in DEKF estimation
$\mathbf{R}^n$	Measurement covariance matrix in DEKF estimation
$\mathbf{R}^e$	Noise matrix in DEKF estimation
S_x	Power spectral density
SW	Small worldness
t_i	Number of triangles
T_i	Number of edges
Thr	Spike threshold
T_r	Transitivity
$\mathbf{v}_k$	Measurement matrix
$V_{c,k}$	Variance coefficient for k^{th} segment
V_c	Variance coefficient critical threshold
$\hat{\mathbf{w}}_0$	Initial weight estimate
$\mathbf{w}_k$	Process noise
$\hat{\mathbf{x}}_0$	Initial state estimate
$\mathbf{X}(z)$	Z-transformation of signal vector
$\mathbf{x}(t)$	State vector
$\mathbf{x}_{k+1}$	Unobserved state vector
$\mathbf{y}(t)$	Signal vector
$\mathbf{y}_k$	Observed signal vector
$\mathbf{Z}(\omega)$	Matrix with real and imaginary components of $\mathbf{A}(\omega)$
$\chi^2_{ij}(\omega)$	Direct-directed transfer function
δ_{c_i,c_j}	Kronecker delta
ϵ_i^E	Exogenous driving signal
ϵ_i^L	Latent signal
ϵ_i	Driving noise
ϵ_{ii}	Element of noise covariance matrix
ϵ_{ij}	Efficiency
$\eta(t)$	Random noise
$\gamma_{xy.z}$	Partial coherence between signal x and y
$\gamma_{ij}(e^{j\omega})$	Directed coherence from signal x_j to signal x_i
γ^2_{ij}	Directed transfer function
$\lvert\pi_{i\leftarrow j}(w)\rvert$	Partial directed coherence
σ_p^2	Prediction error for a model with order p
σ_x	Standard deviation of signal x
σ_x^2	Variance of Signal x
σ_{ij}	Element of cross covariance matrix
σ_n	Estimate of standard deviation of background noise

ρ_{xy}	Correlation coefficient between signal x and y