COMENIUS UNIVERSITY IN BRATISLAVA
FACULTY OF MATHEMATICS, PHYSICS AND INFORMATICS

MATHEMATICAL TECHNIQUES TO REVEAL COGNITIVE MECHANISMS OF AUDITORY LOOMING BIAS

Diploma thesis

2022 Kevin Purkhauser

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Study Programme: Cognitive Science

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Department: Department of Applied Informatics

Supervisor: doc. RNDr. Martin Takáč, PhD.

Consultant: Mgr. Róbert Baumgartner

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THESIS ASSIGNMENT

Name and Surname:	Kevin Purkhauser
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Title: Mathematical techniques to reveal cognitive mechanisms of auditory looming bias

Annotation: Most of the previous studies in acoustics haven't distinguished between the influence of motion, or intensity with respect to sound sources, that are acting on cognition. Recent studies demonstrate that there is a difference of motion and intensity when it comes to processing sounds. This thesis aims to use this new insights and extend their findings by interpreting them mathematically and discuss outcomes in a valuable scientific manner.

Aim: 1. Describe previous experiments (foremost: Baumgartner 2017) on auditory looming bias.
2. Undergoing connectivity analysis of the empirical data by exploring different mathematical tools, like Granger causality, or phase transfer entropy (PTE).
3. Discuss the implications of the processed data and its possible insights on neural and cognitive mechanisms.

Literature: Baumgartner, R. et al. (2017): Asymmetries in behavioral and neural responses to spectral cues demonstrate the generality of auditory looming bias, in: PNAS 114, 9743-9748.
Georgescu, M. et al. (2021): Mathematical Modeling of Brain Activity under Specific Auditory Stimulation. Computational and Mathematical Methods in Medicine 1748-670X

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Declaration

I hereby declare that I elaborated this master’s thesis independently without any unauthorised third-party support. Used literature and ideas taken from other sources are cited as such.

Bratislava, 2022

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Above all, there was a chain of opportunities that had not yet been realised. Sheer potentials far from my sphere of influence, that manifested due to external impact and made all of this not only possible, but real in the sense we refer to as reality. So for most I want to thank my family for making me possible, geno- and phenotypically.

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Abstract

(Somewhere in and around you: cognitive chirping) Yes? Uh-huh. So you can hear that too? Right as you are reading these lines, this sound in your head? ... and could you tell whether it is approaching or moving away from this strange being you are used to calling "you"? This thesis offers an interdisciplinary perspective on the cognition of hearing. Scientifically in more detail: on the mathematical interface between auditory cognition and neural activity, which culminates in connectivity analyses. Recognising sounds from an arbitrary environment and processing them mentally, requires a highly complex cognitive system. Not only for the subject that processes, but also for the scientists who describes such processes. However, previous empirical work (Baumgartner, 2017) investigates in the phenomenon known as "auditory looming bias", which states that listeners are more sensitive to approaching sounds (*looming*), compared to receding ones. Whether this effect - explained as product of evolutionary pressure - is a perceptual bias for changes in distance, or a direct reaction to sound intensity, remains to be controversial. Nevertheless, this study tested subjects in multiple scenarios with looming sounds, thereby measured behaviour and electroencephalography, while listeners judge motion direction. As a result, looming bias occurs as reaction to perceived motion in distance, rather than distance itself. This means that a threat of distortion can be brought about by changing the spectral cues while keeping the intensity constant. Astonishingly, this is only the case when the stimulus is continuous and uninterrupted over time. Given the empirical data, this thesis builds on and compares quantitative, as qualitative methods like Granger Causality (GC), Dynamical Causal Modeling (DCM), or Phase Transfer Entropy (PTE). In doing so it enables a more detailed exploration of the mathematical tools to unfold cognitive and neural mechanisms of auditory effects on human plasticity. Therefore the thesis ranges from i) an introduction of the history and fundamentals of auditory cognition, including an explanatory reflection of the experiment (e.g. auditory tests, EEG, MRI) ii) an identification parade of the mathematical tools that transcribe neural dynamics iii) a discussion of the implications on auditory plasticity iv) suggestions for further investigations within this area v) picking up the introducing question, a critical discussion on the influence of temporal- and spatial continuity for the process of hearing and processing of metrics in neuro-/cognitive science. Finally, this means the thesis combines aspects of physics, acoustics, mathematics, psychophysics, epistemology, auditory neuroscience and physiology of hearing, in order to enable an inter-, multi- and transdisciplinary exploration of auditory cognition.

Keywords:, neuroscience, granger causality, transfer phase entropy, auditory looming bias, EEG, cognition

General Terms: attention, acoustic, auditory cognition, hearing, computationalism, grounded cognition, multimodality, psychophysics

Abstrakt

(Niekde vo vás a okolo vás: kognitívne cvrlikanie) Áno? Mhm. Takže to tiež počujete? Práve keď čítate tieto riadky, tento zvuk vo vašej hlave? ... a vedeli by ste povedať, či sa približuje alebo vzďaľuje od tejto zvláštnej bytosti, ktorú ste zvykli nazývať "vy"? Táto práca ponúka interdisciplinárny pohľad na poznávanie sluchu. Vedecky podrobnejšie: na matematické rozhranie medzi sluchovou kogníciou a nervovou aktivitou, ktoré vrcholí analýzami konektivity. Rozpoznávanie zvukov z ľubovoľného prostredia a ich mentálne spracovanie si vyžaduje vysoko komplexný kognitívny systém. Nielen pre subjekt, ktorý spracúva, ale aj pre vedcov, ktorí takéto procesy opisujú. Predchádzajúca empirická práca (Baumgartner, 2017) však skúma fenomén známy ako "auditory looming bias", ktorý hovorí, že poslucháči sú citlivejší na blížiace sa (looming) zvuky v porovnaní so zvukmi vzďaľujúcimi sa. Zostáva sporné, či tento efekt - vysvetľovaný ako produkt evolučného tlaku - je percepčným skreslením pre zmeny vzdialenosti, alebo priamou reakciou na intenzitu zvuku. Napriek tomu táto štúdia testovala subjekty vo viacerých scenároch s blížiacimi sa zvukmi, čím sa meralo správanie a elektroencefalografia, zatiaľ čo poslucháči posudzovali smer pohybu. Výsledkom je, že skreslenie pri loomingu sa vyskytuje viac ako reakcia na vnímaný pohyb vo vzdialenosti než na vzdialenosť samotnú. To znamená, že hrozbu skreslenia možno vyvolať zmenou spektrálnych podnetov pri zachovaní konštantnej intenzity. Prekvapujúce je, že to platí len v prípade, keď je podnet kontinuálny a neprerušovaný v čase. Vzhľadom na empirické údaje táto práca vychádza z kvantitatívnych, ako aj kvalitatívnych metód, ako sú Grangerova kauzalita (GC), dynamické kauzálne modelovanie (DCM) alebo entropia fázového prenosu (PTE), a porovnáva ich. Umožňuje tak podrobnejšie skúmanie matematických nástrojov na rozvinutie kognitívnych a nervových mechanizmov zvukových účinkov na plasticitu človeka. Preto sa práca pohybuje od i) úvodu do histórie a základov sluchového poznávania vrátane vysvetľujúcej reflexie experimentu (napr. sluchové testy, EEG, MRI) ii) identifikácie matematických nástrojov, ktoré zapisujú neurálnu dynamiku iii) diskusie o dôsledkoch na sluchovú plasticitu iv) návrhov na ďalšie skúmanie v tejto oblasti v) vyzdvihnutia úvodnej otázky, kritickej diskusie o vplyve časovo-priestorovej kontinuity na proces počúvania a spracovania metrík v neuro-/kognitívnej vede. Práca spája aspekty fyziky, akustiky, matematiky, psychofyziky, epistemológie, sluchovej neurovedy a fyziológie sluchu, aby umožnila inter-, multi- a transdisciplinárne skúmanie sluchového poznávania.

Kľúčové slová:, neuroveda, Grangerova kauzalita, entropia fázového prenosu, sluchové skreslenie, EEG, kognícia.

Všeobecné pojmy: pozornosť, akustická, sluchová kognícia, sluch, komputacionizmus, podložená kognícia, multimodalita, psychofyzika

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Most important abbreviations

ALB Auditory looming bias

DCM Dynamic causal modelling

EEG Electroencephalography

fMRI Functional magnetic resonance imaging

GC Granger causality

HRTF Head transfer function

PAC Prefrontal auditory cortex

PFC Prefrontal cortex

PTE Phase transfer entropy

1 Introduction

As an introductory appeal, I like to start this work with a historical foray not only through acoustics, or connectivity in its modern phase, but to the versatile elements that go far back in the history of science. The following chapter therefore describes constitutive pillars of physics, music, mathematics, dressed in the coat of instrumental developments up to cultural music, as they have partly evolved in parallel with scientific breakthroughs.

1.1 Historical Walkthrough

Akoustos, greek for heard, nowadays known as *acoustics*, deciphers as the science of production-, control-, transmission-, reception- and effects of sounds. Hence, beside the plangent sounds that were used in battlefields in order to terrorise enemies and the rather lenient aspects of musical evolution - primarily through pounding of stretched out animal skins or plugging bow strings - the fascination for the orchestrated phenomenon of physical waves, physiological responses and psychological effects reaches far back. That forms a society wherein language through verbal expression catalysed into singing, gesturing and movement of the body to certain rhythms emerged to dancing and early blow instruments were carved out of animal horns, before later wind instruments where made by evolved metal forming techniques.[1]

Long before that, the potential founders of something like music reaches back to ancient China: Ling Lun and Kui. Lun created the first flutes by cutting bamboo sticks in five pieces, equivalent to today's *do, re, mi, sol, la*. Kui on the other hand stretched animal skin over a jar to build the very first drum.[2] The resulting twelve notes, supported by the rhythm section, enabled first performances in composing. Worth to mention that the subdivisions of an octave varies in different countries and cultures among the globe. For instance, the ancient Hindus systemised music by twenty-two notes. The Arabs meanwhile subdivided an octave into seventeen steps. More scien-

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[1] Animal horns were fashioned into musical instruments (the Bible described the ancient Israelites' use of shofarim, made from horns of rams or gazelles, to sound alarms for the purpose of rousing warriors to battle

[2] Lihui Yang and Deming An, with Jessica Anderson Turner, Handbook of Chinese Mythology. Santa Barbara, California: ABC CLIO, 2005, p. 159.

tific approaches of sounds that led to unite cultural differences were followed by feasible investigations.

1.1.1 Ratios

Besides looking at acoustics from a more cultural or musical side, the study of water waves proved to be a useful tool, not only for the ancient Greeks, but for science in general, even to this day. Pythagors (550 BC) was one of the first who invested in this particular realm. Aiming to harmonise things by putting them in tune, Pythagoras used a monochord, which is basically a string - variable in length - stretched over a cuboid resonance body. The function of the length, known as pitch, could get represented by subdivisions of the string, like 1/2 (octave), 2/3 (fifth) and so forth. Adapting this findings to ethics, astrology and literally everything, Pythagoras concluded: "*everything is number*". The world is driven by harmony, governed by the laws of order, which are essentially expressed as ratios. Through the further development of his studies on the physical effects of sound waves on biological or psychological systems, the brilliant discipline of acoustics began to emerge.

Our modern system of tuning and understanding the harmonic structure of ratios is widely attributed to a rich and interdisciplinary progression of various scientists, engineers, musicians and many others. Anyhow, another milestone, which still stands toady, was the explanation of sound as compression and dilution by Aristotle (350 BC). An insight with great impact, as sounds became useable to engineers like Vitruvius (20 BC) who implemented acoustics in space and in the architecture of theatres as he installed segments of resonance by placing rows of large empty vases.

Besides the architectural aspects, it happened in the 6th century AC, as the Romanian philosopher Boethius draw relations between science and music to come up with suggestions about the human perception of pitch and its relation to the physical property of frequency, all in one vase. Like Pythagoras did before, Boethius understood the value of ratios and knew how to apply them in a variety of ways.

Another groundbreaking discovery came with the need for some kind of medium in which sound can propagate. Similar - albeit by far less confusing - to the long lasting controversy about the constitutive medium of light and gravitation, it was hypothesised that sounds can only propagate in a flexible medium. Leonardo da Vinci (1452-1519) stated that there is no sound if there is no movement of air which brought him to the idea that sound waves are much more like water waves and thereby concluded that the sound must have a definite velocity. Leonardo was also involved in the discovery of sympathetic resonance, stating that generic vibrations excite further vibrations, depending - again - on their ratios.

1.1.2 String laws

Almost 2000 y. after the monochord and 3000 y. after the bamboo flutes, the modern science of acoustics presumably elevated to more sophisticated levels by the mind of Galileo (1564-1642), who summarised in concise manner: "*Waves are produced by the vibrations of a sonorous body, which spread through the air, bringing to the tympanum of the ear a stimulus which the mind interprets as sound.*"[3] Soon after, in what could be called the real origin of psychophysical acoustics, the first measurements of the speed of sound were successfully accomplished by a human detector. A prominent scientist at the time was Mersenne (1588-1648) who studied the monochord in many different ways. Further progress came with *Harmonie universelle* (1636), wherein Mersenne studied vibrations of stretched strings and summarised his findings in the three following laws[4]:

1. The fundamental frequency (FF) of a string is inversely proportional to the length of the string, at constant tension and mass per unit length:

$$f_1 \propto \frac{1}{L}$$

2. The FF is directly proportional to the square root of the tension in the string, keeping length and mass per unit length of the string constant:

$$f_1 \propto \sqrt{F}$$

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[3] Crocker, Malcolm J., ed. (1997). Encyclopedia of Acoustics (4 volumes). New York: J. Wiley & Sons.

[4] Wolfgang Köhler: *Die Blasinstrumente aus der „Harmonie Universelle" des Marin Mersenne.* Übersetzung und Kommentar des „Livre cinquiesme des instruments à vent" aus dem „Traité des instruments". Moeck, Celle 1987

3. The FF is inversely proportional to the square root of the mass per unit length of the string, given a constant length and tension of the string:

$$f_1 \propto \frac{1}{\sqrt{m}}$$

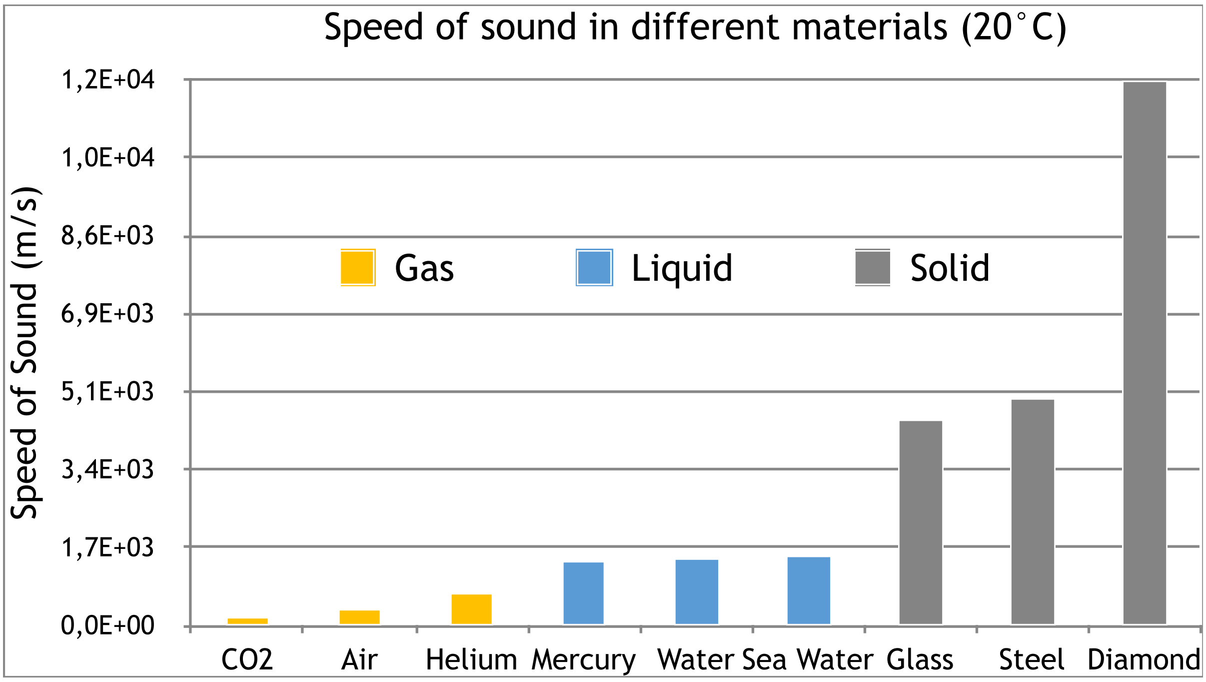

Figure 1: illustrates the speed of sound (20°) in different materials, separated in three different aggregates: gas, liquid, solid. On the right end, beside diamonds would follow solid hydrogen: 4,0E + 04, resp. 36000m/s. On the left end in a perfect vacuum the technical sound speed of 0 would be reached. Which still seems to be an asymptotic challenge, since perfect vacuum is unreachable, but even if, quantum effects like the Casimir effect, or others would appear and describe the sound range closest to 0.

Mersenne used different materials and changed the thickness of the strings in order to stretch the strings out up to several meters. Although, ironically, it then became an almost silent experiment, after all, such heavy strings would hardly have produced an audible sound frequency given their length. However, Mersenne allowed counting the frequency to find the prime ratios and extrapolated them to tone scales. From this he concluded that sound propagates as a wave and not as a particle or somewhat similar. Since this premise seemed to be true, the wave of a sound packet must also be measurable.

1.1.3 Speed of sound

French philosopher and scientist Pierre Gassendi (1592-1655) did measure the speed of sound by comparing the time difference between spotting the flash of a gun and hearing its report over long distances. At that time Gassendi measured 478.4 m/s and correctly implicated that the speed of sound develops independent from its frequency. It took almost 50 more years to do better. It was Mersenne who broke the records and measured the speed of sound using slightly different techniques. Most efficiently by measuring the time an echo takes to reflect the phrase *„Benedicam dominum"*, which was spread out on a wall. By measuring 316 m/s the deviation from modern measurements was less than ten percent.[5]

After first breakthroughs in physics, sound was measured and compared in different materials, subsumed in the three known aggregates (see fig. 1). [6]

How fast sounds can go depends on the medium, not on the sound. Hence neither its amplitude, nor its frequency matters to make any difference in speed. In the case of gas what does matter is the temperature and the molecular mass. Helium has much lighter molecules than air, which triples triples its sound speed. Additionally sound travels faster in warmer, than in colder air. Anyhow for solids it is a different and much faster undertaking. Since the medium of solids is not squashed and stretched in a classical way, vibrations of phonons carry the sound wave. For diamonds it reaches about 12000 m/s. This is about one third of the approximated theoretical maximum of sound speed in solid hydrogen of about 36000 m/s. Sound is produced by the prop-

[5] Thats not all. For instance on Mars, where it is significantly colder than on Earth, sound takes longer to travel, which is about 241 m/s. Besides, the atmosphere is 100 times less than Earth, which makes the sound "softer".

[6] Exciting enough, but not part of this work, to take a moment and reflect on other aggregates, investigating in the speed of sound in plasma, or Bose-Einstein condensate, where density waves in a condensate determine to a function of temperature only, which stays in good agreement calculations of Landau two-fluid models (see: R. Meppelink, S. B. Koller, and P. van der Straten,Phys. Rev. A 80, 043605 – Published 12 October 2009), or instabilities in the Kronig-Penney potential (see: Dong, X., Wu, B. Instabilities and sound speed of a Bose-Einstein condensate in the Kronig-Penney potential. *Laser Phys.* 17, 190–197 (2007)).

agation by making neighbouring particles interact with one another. Atoms can only move as fast as the density of a material and the atomic bond limit this process.[7]

Simultaneously theoreticians developed the mathematical formulas that describe the behaviour of waves through space and time. Just after the invention of standard analysis calculus (Newton & Leibniz, et al., in the late 17c.) it became feasible to derive the laws of waves. The likes of Euler (1707-1783), Lagrange (1736-1813) and d'Alembert (1717-1783) followed to describe the nature of waves as mathematical functions, evolved and applied the wave calculus to strings, oscillators and other vibrating systems. Poisson and Clebsch brought these studies even further by using membranes instead.
The complex problem of analysing waves in their spectral components was solved by Fourier and the famous Fourier theorem.[8] Later on Ohm came up, who connected the sensitivity of the ear to amplitudes, but not yet the phase of harmonics (Ohms law of hearing).[9]

1.1.4 Helmholtz, Vacuum and Psychophysics

Although a few scientific breakthroughs that have already been mentioned played their parts, this one was perhaps the most important when it comes to psychophysic, conducted by psychophysisist Hermann von Helmholtz (1821-1894) and his book: *On the sensation of tone as a physiological basis for the theory of music* (1836). Accordingly it can be cautiously asserted Helmholtz was the most influential scientist in the field of psychophysics and physiological acoustics until this time. Highly renowned are the Helmholtz resonators, functioning as representers of the auditory system:

"The air mass of such a resonator in connection with that of the auditory canal and the eardrum forms an elastic system, which is capable of peculiar vibrations. If one ear has been blocked

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[7] One step further, but not part of this thesis are analogies between black holes and phonons, called *sonic black holes*. See: *Marion Cromb, Graham M. Gibson, Ermes Toninelli, Miles J. Padgett, Ewan M. Wright, Daniele Faccio: Amplification of waves from a rotating body. In: Nature Physics. 22. Juni 2020, S. 1–5. Arxiv*

[8] A mathematical theorem stating that a periodic function *f(x),* which is reasonably continuous, may be expressed as the sum of a series of sin(x) or cos(x) terms, which is then called the Fourier series. Each of which has specific amplitude and phase coefficients known as *Fourier coefficients*.

[9] Ohm, G., Annalen der Physik (1843) 59 513

(preferably with a sealing wax plug, which has been shaped according to the shape of the auditory canal) and if such a resonator is placed next to the other, one hears most of the tones that are produced in the environment much more muffled than usual; if, on the other hand, the resonator's own tone is given, it crashes into the ear with tremendous force.
This enables everyone, even with a musically inexperienced or hard-of-hearing ear, to hear the relevant tone, even if it is rather weak, from a large number of other tones ..."[10]

Additionally and more or less parallel to Helmholtz - *through a rotating cog wheel* - physicist Robert Hooke produced a sound wave of known frequency. Nowadays, known as the Savart-Wheel (or Disk), which was primarily developed in the 19s.

Long-lasting controversy and misinterpretations was caused by the bell-in-vacuum experiment, where the question was asked: *in what kind of supplement, sub-ground, or medium sound propagates through?* For the bell-in-vacuum test a ringing bell gets located in a jar. Meanwhile the air is pumped out of the jar and the sound diminishes until it becomes inaudible. For long this was recognised as clear evidence for the necessity of a traveling medium. Kircher, a german scholar, retested this later on, still heard a sound and wrongly suggested that air was not needed to transmit sound. Finally Robert Boyle brought this myth to an end by improving the vacuum technology, while he could measure the sound intensity dropping and decreasing virtually to zero, while pumping out the air. From this he concluded that air is a necessary component of sound to propagate.
However, even with more modern ultra-vacuum pumps, enough air molecules remain in space to spread sounds. Therefore, the cause of inaudible waves is seen in impedance, which defines the difference in density between media, in the case of air the density between solids, rather than the absolute lack of air.[11]

1.1.5 Traveling waves in the cochlea

[10] Helmholtz, Hermann F. L. von. 1877. *Lehre con den Tonempfindungen*. Braunschweig, Wiesbaden: Vieweg

[11] More precise questions about air-less sounds, must answer the question about density probability functions.

More modern findings revolutionised the understanding of the functioning of the ear and developed with the achievements of Georg von Békésy, who elaborated the traveling wave theory of the basilar membrane, with the aim of explaining the hearing process in the inner ear. Békésy described the phenomenon by so called „traveling waves“ in the cochlea (snail) of the inner ear, in which a frequency-location transformation takes place.

“… at low frequencies the maximum of the traveling wave is at the tip of the snail, at high frequencies at the snail's base near the oval window…“[12]

This traveling wave theory, which was invented about 70 years ago, is now complemented by a new cellular amplifier theory (cochlear amplifier). According to this theory, the one amplifying component is the outer hair cell, which selects amplitude and frequency of certain sound vibrations by electromechanical feedback.
From the first century B.C. to ultrasound technology in science, medicine and industry in the 21st century, psychophysically both the details of sound - i.e. the physical study of waves (vibrations) - and physiologically above all the ear as an anatomical entrance and further the complex neuronal tunnel system of the auditory cortex evolved tremendously. Since there are several important aspects to get a complete picture of this research area, additional insights in each area are an integral part of this work.

—> *Time line of the* ***acoustical revolution (550BC -> 2019)***

- ***550 BC: Pythagoras; vibrating string***
- ***350 BC: Aristoteles; sound as compression and dilution***
- ***20 BC: Vitruvius; acoustic in space and architecture***
- ***1500: Da Vinci; movement of air***
- ***1600: Galileo; psychophysical origin***
- ***1650: Huygens; sound as a wave phenomenon***
- ***1750-1800: Bernoulli, d’Alembert, Euler, Lagrange, Euler publishes wave equation, Child visualises plate modes***
- ***1850: Helmholtz; sound-sensitivity***
- ***1900: Rayleigh; Theory of sound; surface acoustic wave***

[12] Georg von Békésy: Experiments in hearing. New York 1960

- *1910: Barkhausen; volume measurements*
- *1920: Sabine; architectural acoustics*
- *1932: Tamm; phonons*
- *1948: Bekesy; "wavetrains", cochlea amplifier (first proposed 1948 by Gold)*
- *1970: Sonorous clicks are used to classify bats*
- *1987: Carello, & Pastore; Perception*
- *1990: First acoustic study with discriminant function analysis*
- *1992: Guski; Acoustic Tau - Audition as warning system*
- *2008: Bach et al.; An intrinsic warning cue activating the amygdala*
- *2018: Baumgartner; Auditory looming bias*
- *2019: Safari-Naeini; quantum microphones*

1.2 Information boxes for used parameters

Hearing of sound

Cochlea	consists of three fluid filled sections, which serve as a sensor for pressure variations	Outlets between these sections lead to mixtures of the fluids and impairment of hearing
Hair cells	Outer: active element, non-linear amplification of quiet sounds	Inner: movement transforms in a neural answer
Basilarmembrane	Bekesy discovered wave-like distortion that travels along B.m.	Frequenz analysis, non-linear
ITD	Timedifference between right and left ear	Enables auditory circuitry to process locations
ILD	Difference in amplitude	More dominant at low frequencies

HRTFs	Head related transfer function	Spectral cues, ITD, ILD

Physics of sound

Amplitude	Pascal	[Pa]	Soundpressure
Frequency	Hertz	[Hz] **$\omega/2\pi = ck/2\pi$**	Vibrations/second
Wavelength	**Lamda**	[λ] c/f	Velocity/Frequency
Phase	Rad	[φ]	
Impedance	**$Z(\omega) = \hat{p}(\omega)$**		**$\hat{f}(\omega)$ is the fourier-transformed of $f(t)$**
Soundpressure			**$p(x, t) = \partial u(x,t) / \partial t$**
Speed of sound	M/s	**c: global velocity of the pressure wave**	**Speed of sound ≠ particle velocity**
Particle velocity	**Velocity potential: $u(x,t)$**	$v(x)$: Local velocity of particle	**$v(x,t)=\nabla u(x,t)\cdot n(x)$**
Huygens-Fresnel principal			**Every point of a wavefront is the origin of a new wave**

1.3 Structure and Aim of the thesis

Indeed, this thesis claims to be eclectic. Following a nowadays rather unconventional historic introduction - at least to this extend - this enquiry continues by fusing features of physics, neuroscience, physiology, mathematics, computationalism and auditory cognition. In many ways, given the multifaceted character of neuroscience, this is quite conventional. Thereof, in the endeavour to cross lines of demarcation, this thesis may provide unusual interactions, which in turn afford inconvenient reflections. At least the theoretical part is prone to swerve at times, whereby the practical experiments tend to ground. In general this thesis captures both parts and aims to bring them together.

One basic and fundamental question, that motivated this thesis at first place, can be posed as: *"What is the role of brain connectivity analysis and how is it functioning deep down?"* Starting from there, further queries follow as *"What does modelling electromagnetic waves in their pure mathematical form reveal about organic entities like the brain?"*. *"What is the relationship between an acoustic-cognitive model and different types of statistical formulas?"*. *"And isn't there another way to make that possible?"*. An overview of basics, modern models, conjunctive experiments, and further considerations condenses the structure of the thesis in the course of prompting responses to scientific questioning.

Primarily the thesis starts with explanations of fundamentals. For the sake of order, Chapter 2 is separated into 3 sections. Sec. 2.1 explains the physical background of sounds, including wave characteristics and mathematical expressions. Although this barely touches the apparent content of the thesis, it is one of these underlying veins, that becomes all too relevant when asking deeper questions about the complete corpus of connectivity later on. Continuing with sec. 2.2, basal physiological elements are discussed. In terms of the incremental approximation near the core content, this part already deals with functionings of the ear and phenomena of hearing. Brought one step further, sec 2.3 treats the processing of sound through cortical areas.

After this follows chapter 3 which brings the fundamentals together, so that a model of acoustic-cognitive processes can be described. As a matter of research and complexity, there is no single model to name. Consequently, I draw the most relevant models that explain acoustical pathways in the brain, in order to clear up the melange and expose the most vivid aspects in respect to this thesis. Sec. 3.1 introduces by conceptual clarifications, that abet to disclose the intentions of acoustic-cognitive modelling. Subsequently (section 3.2), the role of auditory cognitive effort - also known as listening effort - is defined as the increased allocation of available cognitive resources that can lead to improvements in listening tasks. Then, sec. 3.3, I examine neuroscientific layers and grave interlinks for the resultant connectivity analyses. Finally, sec. 3.4 closes the chapter by evaluating the more recent status of the acoustic-cognitive modelling.

In accordance with the first three chapters, 4 - 6 delivers the principal constituents of the thesis. Starting with the experimental part (chapter 4) on which the thesis is based on and diffuses from (4.1 introduction, 4.2 materials (experimental design), 4.3 results, 4.4 discussion). Chapter 5 goes into detail regarding brain connectivity analysis (5.1 Multilayered architecture, 5.2 Networks and graphs, 5.3 Connectivity measures, 5.4 Connectivity metrics, 5.5 Synchronising connectivity). This involves examination of neuronal architecture and their algebraic equals, as the difference of segregation and integration that leads to the threefold classification of connectivity. Chapter 6 follows, in which three of the most commonly used and best established models for analysing neuronal connectivity are derived in detail, explained and their limitations highlighted (sec. 6.1 - 6.3). Of particular interest is the diversity of mathematical methods regarding analysing connectivity patterns in the brain. Sec. 6.4 concludes the chapter with a comparison of the three methods.

From modelling, experimental, through computational, to mathematic-analytical, chapter 7 completes the content area of the thesis by qualitative implications, limitations, pitfalls and reflections on scientific relations, as possible denouements (7.1 Current methods, 7.2 In-between connectivities, 7.3 Behavioral integration, 7.4 Cognitive modelling).

To finalise the whole venture, chapter 8 adds a summary and last remarks. Chapter 9 contains the references and the brings the thesis to an end.

2 Fundamentals

The fundamentals here are tautological to form the fundament. Since the first steps in our perception of sounds and what sounds most likely are, is very well understood, the following pages collect some important aspects of this well established state of knowledge. As it goes on, it gets more and more interesting, especially when it comes to the brain and how sound is processed in the cortex, because that's where things get fuzzier and fuzzier. Of course, this is not to say that the essence of sound is unquestionably clarified. Considering that matter is involved and whether matter is itself some kind of wave, energy, or even frequency multiplied by some fundamental constant ($E=hv$), states of knowledge are constantly changing. Depending on how closely one wants to examine the essential components of sound, one can arrive at strange descriptions that say that sound is a wave above another wave or a frequency within a frequency. Which again is most likely the case, but not in a way that would cause a direct mutual influence that can be investigated at this stage. Furthermore, when describing interaction phenomena, it always depends on which scale the region of interest is focused on. At this stage, we are starting with the fundamentals.

2.1 What is sound?

To start things off we could ask the question: *What is sound?* One answer might be: *Sounds are nothing more than audible*[13] *variations in air pressure*. This is principally a consequence of mechanics and a description of gases that propagate in gas, liquids, or solids. In that, sound is a fundamental branch of mechanics and formalised in terms of Newton's laws. Almost anything that can move molecules (vibrate) can generate sounds. As a result, whenever an object moves towards a patch of air it compresses the air, thereby increases the density between the molecules. Conversely the air is rarefied, meaning it decreases its density as soon as an object moves away again.

Many sound sources produce air pressure fluctuations that follow different patterns, e.g. rhythmicity. An important component of which is the speed of pressure waves, that can reach about

[13] At least most of the time, if not exclusively

344 m/sec at room temperature (293,15 K) and 50% relative humidity.[14] Imaging the mapping of two sound sources not having exactly the same frequency, hence interfering with the crests and at times with the crest and the trough. These interferences in time can get recognised as beats. For what it's worth the frequency of the sound is the number of compressed or rarefied patches of air that passes by our ears, every second. This means that the speed of a sound wave propagating in the air is almost independent of its frequency.

2.1.2 Propagation of sound

At this point, let us delve a little deeper into the physics of sound. When an object moves from one place to another through space, it causes a change in pressure in the medium in which it moves. With the compression taking place, additional changes of pressure are caused, which in turn lead to a consecutive arrangement of pressure changes that propagates forth and can be described by wave mechanics. Anyhow, this is not yet sound. To produce an audible exchange of pressure, the areas where the pressure and density changes occur must be larger than the areas where the molecules previously collided. This is when molecules from a higher pressure or density crash into their neighbors with a lower density or pressure and give them momentum. Thus, the distance between crest and trough of the pressure wave needs to be larger than the distance of the mean free path. In its most simple case, one-dimensional (x) and almost plane wavefronts, the generic formulation of such a phenomenon leads to a displacement of molecules through time (t). Hence the sound wave can be described as a function: X (x, t).
One important feature of the phenomenon of sound waves is that change in density corresponds to change in pressure. Conventionally pressure is measured in bar. 1bar = 10^5 N/m^2, whereby one 1 atmosphere (atm) roughly equals 1 bar (1.0133bar). On the other hand, the acoustic pressure level is scaled in decibel. $20\log_{10}(p/p_{ref})$ in dB.[15] In contrast to the equilibrium state of 1 bar, changes in pressure are utmost small.

2.1.3 Acoustic wave equation

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[14] Bannon, Mike; Kaputa, Frank (12 December 2014). "The Newton–Laplace Equation and Speed of Sound". Thermal Jackets. Retrieved 3 May 2015.

[15] p…mean square sound pressure, p_{ref}…references sound pressure; $20\log_{10}$ since the ear's sensitivity is roughly logarithmic

The following equation is one of the most basic wave equations there is. It is generally known and frequently used. It describes the sound in one dimension (x), propagating through time (t):

$$\frac{\partial^2 p}{\partial x^2} = \frac{1}{c_s^2}\frac{\partial^2 p}{\partial t^2}$$

p… acoustic pressure = ambient pressure deviated by local (position x) pressure
c… speed of sound

2.1.4 Derivation of the acoustic wave equation

The derivation of the equations underlying psychophysics opens up an important insight into the matter. In fact it is nothing else than the change in density as gas moves. Suppose the position $x + \Delta x$ gives the displacement, which we write as χ when disposition depends on x and t, instead of other dimensions in more complex cases (y, z). In connection with ϱ (density), we find that $\varrho\Delta x=\varrho[x+\Delta x+\chi(x+\Delta x,t)-x-\chi(x,t)]$. Inasmuch Δx is small and depends on position and time, parts of χ can be written as partial derivatives. Boiling down to $\varrho=-\varrho(\partial\chi/\partial x)$. This spells the density change if gas moves. More precisely if x increases, meaning the air molecules are stretched out, the density decreases.

Beside the density changes we have to consider pressure changes as well. Acceleration of air molecules, in dependence of position and time can be written as $\varrho\Delta x\ (\partial^2\chi/\partial t^2)$. The force induced by pressure changes pushes in one direction as P(x, t) and in the opposite direction as P(x+Δx, t). Subtracting one from the other we get $P(x, t) - P(x+\Delta x, t) = -\partial P\partial x\Delta x = -\partial \mathrm{P}\partial x\Delta x$

Putting all the features together we find $\dfrac{\partial^2\chi}{\partial x^2} = \dfrac{1}{c_s^2}\dfrac{\partial^2\chi}{\partial t^2}$

Finally we have a formula of the behaviour of sound in matter, described as a wave equation. It interconnects the speed of sound with the density at normal pressure and the rate of change of pressure.

Additionally I like to mention that the speed of sound is not isothermal.[16] Pressure and temperature change adiabatically, so that a slight change of heat does not effect the speed of the sound wave, but its overall energy level. This is of importance when the question gets raised if the speed of sound is equal to the speed of the molecules, that causing the vibration of the ear drum. It turns out that the adiabatic change of heat and the propagation of an audible sound takes longer than the movement of the molecules themselves. Therefore it can be roughly said that half the speed of sound (c/s) approximates the average molecular speed.

High and low frequencies of sound need to be distinguished. Because sound waves all propagate at the same speed, high-frequency sound waves have more compressed and rarefied regions packed into the same space than low-frequency waves.

2.1.5 Sound in the universe

The mechanical nature of sounds are nothing but audible variations in air pressure. Hence inversely if there is no air at all, there won't be no sound neither. Which means in a complete vacuum, there won't be any sound at all and the universe is a pretty quiet place.[17] [18] Apart from that, almost anything that can change the density of molecules may generate sounds.[19] This covers vibrating strings, blows from sticks, windy tubes and the ear itself. Indeed, it is possible and at times the actual case, that someone hears the sound of their own inner ear, which can be quite intimidating and recognised as pathology.[20]

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16 Laplace corrected Newton in this assumption, who wrongly argued that heat is conducted from one region to the next with such a high speed, that the temperature cannot change.

17 Of course there is no absolute vacuum, but inly high-ultra vacuums. Which implicates that there is no place in existence, where there is no sound at all. As quiet as it may be, it can never reach zero.

18 Though the universe seems fairly quiet, there can never be nothing. E.g. listen to the "Chirps" - measured gravitational-waves signals of black holes, converted into sounds (LIGO): https://www.ligo.caltech.edu/video/ligo20160615v2

19 Easy to visualise in the case of stereo speaker, in which a paper cone attached to a magnet vibrates in and out, alternatively rarefying and compressing air.

20 Tinnitus is familiar, but something else.

2.2 The curiosity of hearing

So far we have described sound waves and how they propagate from the mechanical perspective. Next up is to unravel the anatomical side of our most important receiver: the ear.

2.2.1 Anatomical Walkthrough

Starting with the outer ear, the gate for every sound wave penetrating our auditory system is the pinna (which gets more important at the experimental part when measuring HRTFs, sec. 4.1). Sounds emanating from a point source propagate according to the law of the inverse square: $P/(4\pi r^{2}) = I$.[21] Saying, if there are no reflections or reverberations (“free field“), the intensity of sound drops, as the power divided by the distance squared. At two times the distance, the intensity drops to one-fourth, at four times the distance to merely one sixteenth of the original energy. As the intensity varies, the sensitivity does with the size of the pinna. A larger receiver absorbs more of the penetrating energy, which spreads out. Beyond that, the receiver, which is constituted by the structures of the outer ear works as amplifier and may raise the human hearing sensitivity by a factor of 2 up to 3.

Afterwards, sounds that make it through the pinna, onward via the auditory channel. This resembles a closed resonator about 2.4 cm long, enables a frequency peak at about 13 kHz (3rd harmonic of a closed cylinder = 1st harmonic at 4kHz). The onward wave discharges at the 0,1 mm thin eardrum, known as the Tympanic membrane.[22] At the oval window the vibrating drum transfers energy through moving the ossicles.[23] These tiny bones achieve amplification through a combination of leverage that multiplies the force and is adapted through muscle movement. Here it is necessary to add, since it might be important for measurements, that reduction, or exaltation of a sound’s volume is strongly connected to cognitive functions, particularly in auditory neuroscience referred to as attention, or spatial learning. However, at this point it should be noted

[21] Since the inverse square law is a purely geometrical implication, it counts for other propagations as well: gravity, electrical force, radiation, light, etc. Hence it is likewise important

[22] Clark, J. and Martin, F., Introduction to Audiology, Clifton Park, NY: Delmar, 2009.

[23] Ossicles are the three smallest bones in the body: hammer, anvil, stirrup (formally: malleus, incus, stapes)

that hearing is also very much influenced by the current state of the listener due to physiological states. After prolonged listening tests during experiments, the musculature can change its performance due to fatigue or tension. If the test person feels unwell or is in a weak condition, this has an influence on the cognitive apparatus and thus on the measurement. Not least for this reason, shorter experiments, enough breaks, but also the number of test persons is essential for statistically reliable measurements. This will be explored in more detail later on (chapter 7).

Next, the sounds enter the inner ear, which consists of the semicircular canals and the cochlea. The former helps to maintain balance by detecting accelerations in three perpendicular planes and the angular acceleration. These accelerometers make use of hair cells and the canals are further connected to the auditory nerve. The cochlea consists of three fluid filled sections, which serve as a sensor for pressure variations. The fluid perilymph fills tympanic and vestibular canals, as the first two sections and endolymph fills sections three, the organ of Corti. Outlets between these sections lead to mixtures of the fluids and impairment of hearing.

2.2.2 Pitch - Loudness - Timbre

In addition to the basal anatomy, hearing can be divided into 3 distinguishable auditory characteristics (beside space, time and temporal modulations, which are likewise important, but less characteristically auditive). Firstly, pitch is the response of the auditory system to the frequency and quality that enables it to distinguish high (fast vibrations) and low (slow vibrations) tones.[24] This explanation already contains the psychoacoustic challenge for investigations with pitch, since frequency is an objective property of a vibrating system, while a person's reaction to frequency - the pitch - is the subjective perception of a sound wave. Finding a more detailed theory that explains pitch, e.g. place-, or temporal coding, is still a matter of investigation.[25]

Secondly, loudness is related to the intensity of a sound and the amplitude of the sound wave, factored by the ear's sensitivity to the particular frequency the sound actually contains.[26] It there-

[24] For this explanation frequency refers more to frequency patterns, than frequency itself.

[25] see e.g.: Norman-Haignere, et al. 2019, Cheveigné, A. de 2012

[26] Changes of the humans earn sensitivity, as a function of frequency gets illustrated at the equal-loudness graph. (Suzuki, Yôiti; Takeshima, Hisashi (2004). "Equal-loudness-level contours for pure tones". The Journal of the Acoustical Society of America. 116)

fore speaks more for the strength of the perception by the ear than for the intensity of the sound wave itself. One rule of thumb in psychoacoustics states that in order to double the loudness of a sound, its power need to be increased by a factor of ten. This is called the logarithmic relationship of the ears to the sound.

Intensity in decibels: $I(dB) = 10\log_{10} [I/I_0]$[27]. In order to make sense of the subjective sound perception, which varies at different frequencies, the unit phon was introduced. 1 phon equals 1dB given a fixed frequency of 1kHz. Further factorisation ($x^{0.3}$) follows through the unit sone, which equals 40 phon. [28]

Thirdly, if pitch and loudness of sound waves are constant, timbre is another measure that can be distinguished. "*Timbre depends primarily upon the frequency spectrum, although it also depends upon the sound pressure and the temporal characteristics of the sound*“.[29] Timbre refers to the characteristic quality that describes sound by its harmonic content.[30] At the same time, the envelope of sound is important. Since every touch is part of the timbre and changes the envelope, it would be far more difficult to identify a note without a touch, i.e. with a shortened course of sound. Therewith different types of sounds, as voices, or musical instruments can be distinguished from one another, even if pitch and loudness are equal.

2.2.3 Audition

The phenomenon of hearing can also be referred to as auditory perception or audition. Audition, especially in the context of hearing, represents a vivid part of our conscious lives. When certain senses, such as vision, are impaired, other senses, such as hearing, can compensate for the blind spot and loss of visual perception and indeed enable us to recognise presence and identify places. Therefore it can be a powerful accompanist regarding all kinds of cognitive functions, like complex motor skills, or paying attention. While straying through unknown areas, or strolling through the night, strange sounds of rustling leaves, or squeaky metals eventually turn out to

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27 Yost, William (1985). *Fundamentals of Hearing: An Introduction* (Second ed.). Holt, Rinehart and Winston. p. 206

28 double the loudness = double the sone

29 Acoustical Society of America Standards Secretariat (1994). "Acoustical Terminology ANSI S1.1–1994 (ASA 111-1994)". American National Standard. ANSI / Acoustical Society of America.

30 Winckell, Fritz: Music, Sound and Sensation, Dover, NY ,1967.

arouse our attention in a highly intense, or even frightening way and that with evolutionary learned reason. Even more fascinating is the ability to distinguish between sounds and the ability to nuance pitch, so that more complex recognition and reproduction of sounds - such as music - can be cultivated. Just as functions of communication and survival evolved in and outside of societies. More recent scientific studies focus on the cause of hearing, which in most cases turns out to be closely related to cognitive functions, especially the phenomenon of attention and selective perception. According to the latter, listening can be divided into a passive and an active process.

2.2.4 Hearing as an active process

Hearing as an active process and ears as anatomical access points have been considered to be receivers of sound alone. But in fact ears can also emit sounds. With a microphone that is placed sensibly enough, precisely at the faint hum, clear whistles can be picked up in the ear. Consequently, the ears can be seen more as active or reactive receivers, adding additional impulses at the exact frequency one is trying to detect. This concept goes back to Helmholtz, who thought about the hearing organ like a harp as a resonator, made out of strings, that response to intruding air pressure in various ways, depending on the intruding frequency. Instead of strings, the fluid-filled duct of the cochlea, coiled like the shell of a snail, adopted the original idea and brought it further by Gold and later by Kemper. Only to be interrupted by the following experiments of Bekesy.

2.2.5 Basilar membrane

Bekesy discovered the wave-like distortion that propagates along the basilar membrane. The membrane is quite elastic in the longitudinal direction and varies in stiffness laterally, allowing almost independent couplings through the fluid dispersion, which means that the shaft slows down as it advances. Physically a traveling wave can be a simple model of one-dimensional transmission (see sec. 2.1). Hereby the wave sets the cochlea fluid in motion, because of rattling the anvil, stirrup bones and hammer. The incompressibility of the fluid leads to lateral movement of the partially stiff membrane, so the movement of the membrane generates a wave that travels to the apex and produces spikes in the auditory nerve to transfer information about frequency, pitch and the like more.

2.2.6 Hair cells

According to Bekeys rather complex theory of wave mechanics, much is explained, but the finely tuned differences that our ear is able to distinguish remain mysterious. Bekeys himself experimented only on cadavers and needed disproportionate loud sounds to arouse a response of the unaware auditory system. Dead listeners turned out to be extremely inert, in contrast to the living ones.[31] Consequently there has to be an active amplifier that boosts feeble sounds and reduces, or compresses all too powerful ones. The so called cochlea amplifier operates at the brink of the ear organs and located at the more neuronal part of the auditory pathway. At the very least, it's a matter of taste and an ongoing debate about where exactly the ear ends and the brain begins. Therefore one part of the cochlea amplifier, which is more likely to be associated with the ear is discussed right below and the second, more neuronal part, follows in the next chapter.

The amplification process is fulfilled by hair bundles, an assembly of cellular protrusions (stereocilia) and the organelles of the hair cells. These cells function as sensory receptors, detecting movement and transferring varying receptor potentials to active vibrations of the cell body. A distinction for mammals has to be made, as they possess outer and inner hair cells. The outer ones enable a higher sensitivity when it comes to differentiation between frequencies. The motor protein that underlies somatic electromotility is prestin (from musical notation *presto*, meaning fast), which is involved in the exchange in the chloride channels.[32] Electromotility means that the entire cell body contracts when a voltage is applied. Furthermore a composition of stereocilia bend and tip against each other (mechanical response to the environment), which induces a tension gated transduction channel in the cell membrane and changes the ionic current, by changing the cell potential through admitting potassium ions. The hair cells, which convert motion into electrical signals, placed out- and inside the cochlea, are themselves not firing. Rather, they act as sensitive voltage gated receptor channels that open and close in the purpose of trigger-, or releasing neurotransmitters.[33] (see Crawford and Fettiplace, 1985)

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[31] "Sound and Hearing", Stevens, S. S., & Warshofsky, Fred,eds., Time-Life Books, NY, 1965. p54

[32] Santos-Sacchi Joseph; Song Lei; Zheng Jiefu; Nuttall Alfred L (2006-04-12). "Control of mammalian cochlear amplification by chloride anions". Journal of Neuroscience. 26

[33] Chan DK, Hudspeth AJ (February 2005). "*Ca2+ current-driven nonlinear amplification by the mammalian cochlea in vitro*". Nature Neuroscience. 8 (2)

2.2.7 Hopf bifurcation

Hair cell bundles communicate with each other, both outside and inside the cochlea. The critical point of “not too small“ oscillations is known as the Hopf bifurcation. The displacement of the oscillator varies as the cube root of the stimulus force. So as the signal that comes in falls to zero, the gain of the Hopf resonator grows indefinitely. Experimentally it has been shown that displacements of the hair bundles are directly correlated to the amount of decibel. (Variations around 120 dB, displace the hair bundles by only a factor of 100).[34]

2.2.8 Self tuning and feedback control

The mechanism of the self-tuning feedback control, as well as the origin of the oscillations, is still the subject of investigation. Anyhow, the calcium ion influx and the motor protein myosin-1c play key roles in the process. The binding of calcium sensitive, calmodulin to myosin-1c could thereby be responsible to modulate the interaction at the transduction channels.[35]

Another important aspect to mention is shown by the motor components of adaptation. This is split into slow- and fast adaptation. Whereby slow adaptation is superior in vestibular hair cells for sensing spatial movement. It occurs at increased tension by bundle shift, because then myosin-1c glides down the stereocilium, due to decreased tension channels, that are closing and as a response the transduction current diminishes. For fast adaptation, that is superior for hair cells detecting sounds and auditory signals, the tip link tension increases. Ca^{2+} that entered the stereocilium bind rapidly and induce closing the channel.[36]

The curiosity of Hearing (sec. 2.2) is an arrangement of basic scientific achievements designed to disclose the psychophysical process from sound to hearing. Now we go one step further, into the brain, in particular the auditory cord.

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[34] Géléoc GS, Holt JR (2003). "Auditory amplification: outer hair cells press the issue". *Trends Neurosci*. 26 (3): 115–7. (but also Camalet et al., Eguiluz et al.)

[35] Stauffer, E. A.; Holt, J. R. (2007). "Sensory transduction and adaptation in inner and outer hair cells of the mouse auditory system". Journal of Neurophysiology. 98 (6)

[36] Gillespie, P. G.; Cyr, J. L. (2004). "Myosin-1c, the hair cell's adaptation motor". Annual Review of Physiology. 66: 521–45.

2.3 Sound in the brain

Initialised by undulating sounds that travel through space, crossing the ear channel, traverse further to the hair cells and finally propagating into the brain (the demarcation-line between brain and non-brain is still controversial). The auditory nerve serves as first contact, when entering the bridge between the inside and outside world of the perceptual centre. For a longer period of time, traditional models of the neural processing corresponding to hearing described simple features of the auditory system that extract sounds into increasingly complex cortical areas whose functions enable the differentiation, amplification or inhibition of sounds as well as spatial orientation and memory. In recent years there has been an increasing number of studies (one of the latest releases: Hamilton et al. 2021) showing that it seems to be far more unregulated and complex than always assumed. Signals are not necessarily propagating step by step through the brain, but branches into distinct parts of the brain and even jumping back and forth. This assumption is a major step towards finding reasonable explanations for the uniqueness of the brain. In the following we will look at the anatomical and functional line-up of this multifaceted control centre.

2.3.1 Hierarchical framework

The hair cells are responsible for separating frequencies, whereby the separation depends on the position of the cells and additionally hair cells convert ion injections into electrical signals that are caused by movements of the bundles. The electrical signals are then transmitted through the auditory nerve and send through several stations of the cortex as representations of the original sound. All the auditory information that is send to the brain (from inner and outer hari cells) is provided by the spiral ganglion neurons. Likewise these are the first in the auditory pathway to fire action potentials. Interestingly, the outer hair cells outnumber the inner ones by 3 to 1, nevertheless about 5% of synaptic communication happens between the spiral ganglion neurons and the lower numbered inner hair cells.[37] Based on this, it indicates that the brain pays far more attention to the inner- than the outer hair cells. The reason for that might be the amplifying feature of the outer hair cells, already mentioned as the *cochlea amplifier*.

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[37] Kazmierczak P, Müller U. 2012. Sensing sound: molecules that orchestrate mechanotransduction by hair cells. Trends in Neurosciences 35: 220-229

2.3.2 Cochlea amplifier

The ear is not only a transmitter of sound, but also generates it. Two molecular mechanism are found that suggest contributions to amplification. On the one hand, motor proteins are involved so that outer hair cells are not exclusively reacting to receptor potentials, but also change in length. The already mentioned protein prestin - highly packed molecules at the hair cell body - is responsible for the movement of hair cells as a direct response to sound. Also, at the hair bundles, myosin is a possible molecular candidate that is attached to the tip links. In addition there is strong evidence for the described functions of the proteins as certain antibiotics (e.g. kanamycin) may lead to deafness, which is also the case if the genetic encoding of prestin is eliminated (shown with mice) and deafness is the consequence. As the hair cells are attached to the reticular and tectorial membrane, their change of length effects the membrane to be pulled toward or pushed away, thus it guides to the next area of sound processing.[38]

2.3.3 Auditory pathway

For the purpose of this study and with respect to the complexity of the undertaking, the next steps are described concretely and concisely, following one particular pathway rather than describing too much details of all the possible combinations and connections.
As sound (which is less sound, but more electrochemical information by now) is coming from the spiral ganglion, it can meanwhile be considered as transformed information that enters the brain stem through the auditory vestibular nerve. There the axons innervate to the dorsal- and ventral cochlear nucleus. Thenceforth it becomes highly complex, as there are many synaptic branches spreading multidirectional and partially in parallel. Axons from the ventral cochlear nucleus project to the superior olive nucleus, which is located on both sides of the brain stem. Then reaching the inferior colliculus of the midbrain. One the other hand, axons from the dorsal cochlea nucleus are bypassing the superior olive, ascending directly, like all auditory pathways, onto the inferior colliculus. Next stage is in the thalamus and more precisely the medial geniculate nucleus (MGN). Form there it leads to the auditory cortex.

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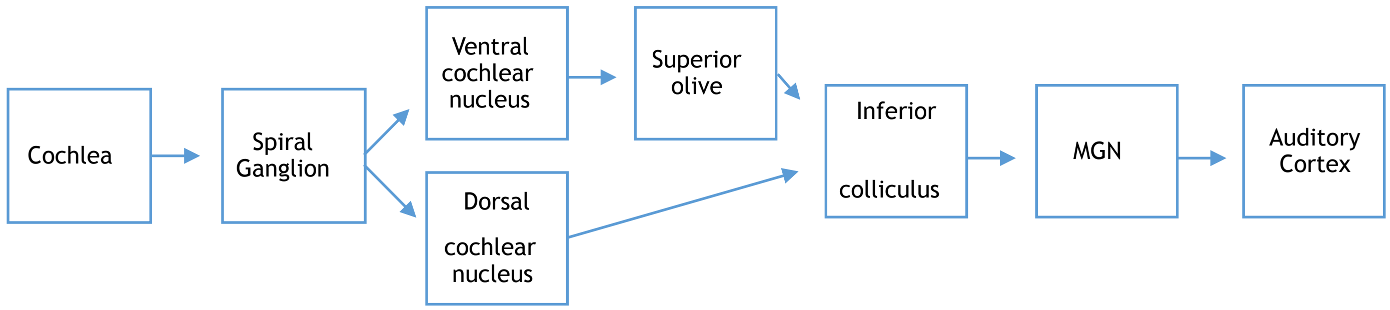
[38] Guinan JJ Jr, Salt A, Cheatham MA. 2012. Progress in cochlear physiology after Bekesy. Hearing Research 293:12-20

The described pathway corresponds the firing rate of neurons as a response to sounds. What is seen in many neurons at each relay, from cochlea to cortex (and back) is the characteristic frequency. That means a neuron is frequency tuned and shows it greatest response at a specific frequency, that bounds the response as characteristic to it. This also means that the threshold of a single fibre of an auditory nerve is lowest, at that particular frequency. At neighbouring frequencies the response is significantly less, which means the threshold remains higher.[39]



Worth noting that the clinical fact of deafness coincides with the auditory pathway of cochlea nuclei, since both cochlea nuclei receive ipsilateral input from one ear. This is just another aspect that shows the complexity of the matter, as the pathway does not only run in one direction as illustrated, but at least with extensive feedback, e.g. from brain stem to outer hair cells, or auditory cortex to MGN as well. Furthermore, forward and backward directions are only part of the whole, as there are also circularities in the different layers that spread out into other geometric dimensions. Despite its relevance, also for the later connectivity analysis, the topology of the brain layers will only play a minor role in the next chapter, which deals with the modelling of auditory processes.

3 Model of Auditory-Cognitive Processing

[39] (see inter alia: Rose, Hind, Anderson and Brugge, 1971)

Modelling, understood as the process of constructing and developing models, which in turn are decoded as conceptual representations of phenomena, is crucial to the sciences of the 21st century. Given the huge amounts of data and the different approaches to dealing with it, it is actually models that make the whole process visible and comprehensible. Furthermore, it creates a tremendous field for scientific work.[40]

3.1 Modelling in neuroscience

With other words, modelling is a creative process that can take many different forms. This includes experimental predictions, summarising discoveries and ideas, making explicit assumptions and the like more. In most cases models are mathematical driven constructs, with which

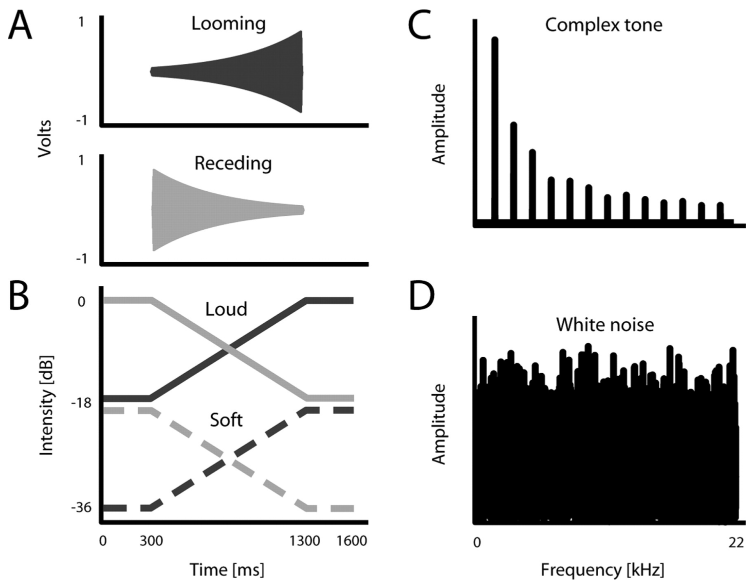


Figure 2: Joost X. Maier and Asif A. Ghazanfar, Journal of Neuroscience 11 April 2007, 27 (15) 4093-4100
Each part of the four-folded figure, represents one measured aspect of ALB. A Time-amplitudes. B Intensity-time, loud=solid lines, soft=dashed lines, looming=dark lines, receding=light lines. C Frequency spectrum of complex tone stimuli. D White noise

[40] Namdar, Bahadir; Shen, Ji (2015-02-18). "Modelling-Oriented Assessment in K-12 Science Education: A synthesis of research from 1980 to 2013 and new directions". International Journal of Science Education. 37

scientists try to describe, or explain observed phenomena within the realm of formulas, that are representations of the real world. Mathematically this includes statistical models, logical models, differential equations, probability models, game theories, or dynamical systems. Listing relatives, or sub-categories of modelling processes raises the question: *what then is not a model?* Which in fact turns out to be a more difficult one, considering the seemingly *pan*-covering territories that models already subverted and partially define. One possible answer could be the context in which it is used as such. Speaking of it in this way says: everything could be a model, as long as it is used as a model. A statistical model already contains "model" in its term, whereby differential equations alone are not sufficient.

Anyhow, in differential calculus we are dealing with continuous changes in time. This is a functional operation and as such already some kind of modelling procedure. Given our physical understanding of the world, time passes smoothly in one direction, instead of jumping back and forth. That is why we can use instruments like clocks and are able to count time as sorts of particles like seconds. In other disciplines, like psychology, or even other physical theories, this is not necessarily the case. So given this juncture we are confronted with a topic in which we can model something that is different in mathematics, relative to other formal concepts and not always coherent with empirical data. Especially at the intersection of mathematics and neuroscience, research that deals with how the brain processes e.g. time and what time actually is, stays curi-

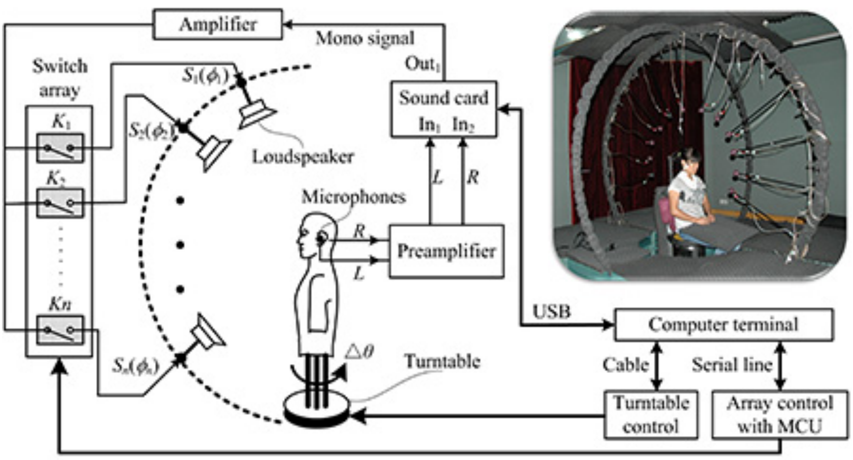


Figure 3: Schema of a Near-field head-related transfer function (HRTF). See: The Journal of Acoustical Society of America 143, EL194 (2018)

ously manifolded. However, in order to account for the continuous changes in time and to create the best possible models, the mathematical tools of the infinitesimal calculus are often used, which are very powerful models.[41]

Formally a model in natural (physical) sciences almost always emerges in similar steps: starting off from basic principles, or (e.g. in classical mechanics) so called balance equations, like the law of conservation. Additionally several classification criteria are commonly added to set weights: discrete vs. continuous, static vs. dynamic, linear vs. nonlinear, explicit vs. implicit, etc. In neuroscience this process develops quite similar. Based on these known constituents, further assumptions - often in the form of quantified parameters - can be tested and implemented. As a result, the modelling process leads to newly defined or simply modified equations. Especially in the natural sciences and the neurosciences, which both branch out into analogue mathematics, there are more similarities than discrepancies. Therefore, it is often helpful to use models that describe phenomena in neuroscience and apply them to describe other phenomena in physics, and vice versa. The next section discusses one of the epistemologically most important theories based on it in the context of modern modelling.

3.2 Ockhams model razor

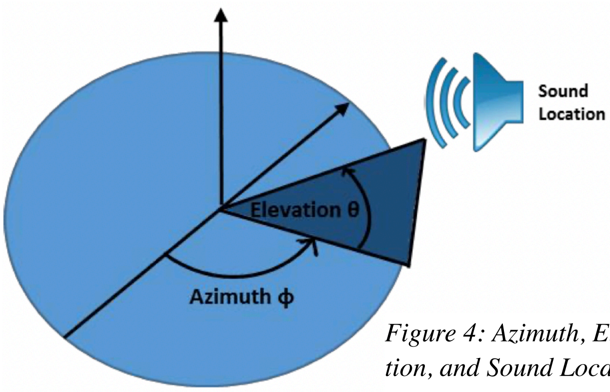


Figure 4: Azimuth, Elevation, and Sound Location Parameters of HRTF

[41] To mention at this point: Calculus is latin and means “stone“, which goes back to the romans, who used stones for counting - again a model. The term prevailed for one of the most striking inventions ever made. Historically it is told that Newton and Leibniz invented calculus almost parallel (before that others were also involved), but completely independent from one another. Not only independent, but their approaches differed, which makes it even more exciting to see only one of two models prevailed (so far Leibniz won this race). Often differentials are explained as “instantaneous rate of change“, but this is obviously an oxymoron. Much more it could be phrased as “rate of change over an infinitesimal small amount of time“ - again a question of the model you pick.

The model itself never represents anything, but merely represents empirical data, observations, ideas or related thoughts in a way that is intended to gain recognition in the scientific community. For example, computer models are now successfully used to simulate dynamics and recognise patterns in large amounts of data, sometimes without even anticipating what the data might reveal beyond. But within certain data sets, one can either know more about the relevant content or make causal statements about internal or external relationships.
More and more virtual experimentation - as another branch of modelling - allows far simpler approaches to earn first intuitions about experimental design, data trials and hidden layers, which are operating in blanked undergrounds. Until today the good old "Ockhams razor" counts, as it shall be the best, meaning the highest explanatory-, but likewise most simpel model that prevails against over-complex, but also over-fitting and sometimes not evenly content-rich competitors. Since the focus today is on modelling, this applies to models as it did to theories back then; hence it could be called "Ockhmas model razor".

Another important aspect is the need to keep clear ideas about the experimental design, the assumed outcome and possible suggestions that other scientists might draw from the ongoing experiment. Therefore models are also forcing scientists to more narrow and also explicit depictions as a means to inter-transfer information. Accordingly models are sharpening ways of communication in the scientific community (Blohm et al., 2020). Since there is hardly any scientific discipline left that works completely untouched by any kind of modelling, this is an opportunity to inaugurate more interdisciplinary activities. A development that is of particular interest for neuro- and cognitive science.

Based on these assumptions and with the aim of discovering something rather than nothing, it is absolutely pivotal to ask the right, most appropriate and contextual questions. In order to deal with data in a constructive and insightful manner, one of the greatest challenges is to engineer useful concepts and build comprehensive models, ideally already beforehand. As precaution to resist the danger of getting lost in a sheer overwhelming sea of data.

Choosing the right model for the right study is not trivial, yet even decisive for the potential development of the study as a whole. In neuroscience alone, there are countless models and modelling techniques, but with new types of data and objectives, it is often not entirely clear how or where to start. This was one of the reasons that led me to look more closely at the mathematical and technical pinnacles of modelling in science. This mainly concerns the methods of connectivity analysis, which I will examine in more detail in section 5.[42]

3.3 Auditory - Cognitive Models

Like there are many ways of modelling, there are various models that have been created to describe auditory functions (Zhang et al. 2001; Lunner 2003; Jepsen et al. 2008; Souza et al. 2015; Wingfield 2016). Auditory-cognitive processing involves spatial awareness, scene analysis, selective attention, attention switching and the ability to specify many different kinds of foci. Some features that are considered cognitive, e.g. memory functions, may occur retrospectively, as followers of auditory and attentional processes. As one can imagine, the timing is crucial for this type of investigation.

3.3.1 Temporal response functions

Using EEG[43] in auditory neuroscience one fundamental aim is to map the cortical responses of brain regions in order to extract the event response potentials (ERP). For continuous stimuli, which you can find e.g. in speech, this is done by temporal response functions (TRFs). While

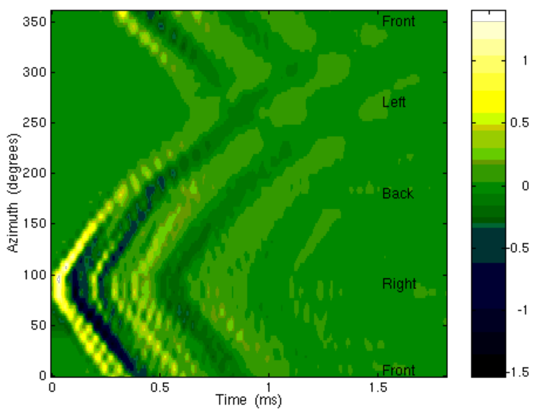


Figure 5: HRIR. In a horizontal plane the right ear (90° azimuth) responses to an impulsive source. Brightness represents the strength of the response, at a point in time. Strongest at 0,4 ms

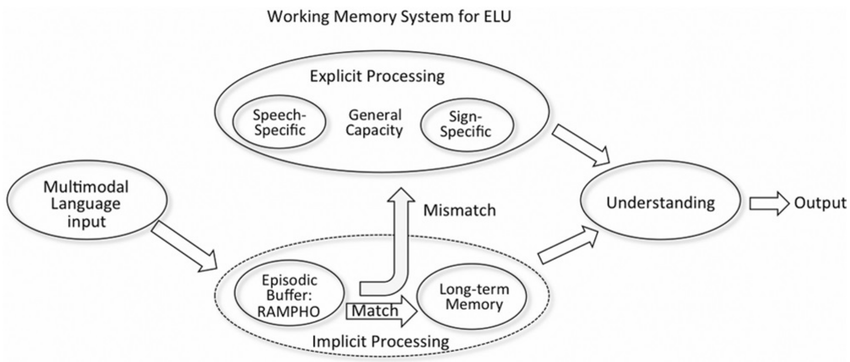
[42] In parallel to my writing of the thesis and experimental work, I joined a CoSMo workshop, which gives valuable insights, like a 10-step orientation guide, for a modelling walkthrough in neuroscience, from which I took a few approaches and integrated some of these into my work.

[43] If not mentioned explicitly EEG and MEG can be used synonymously, since most descriptions are applicable to both techniques.

ERPs characterize the responses of EEG, TRFs generate predictions. Thereon TRFs find a vast scope of applications as stimulus-response models for artificial sound stimuli (Labor et al 2009, Power et al. 2011), phonetical markers at a speech spectrogram (Broderick et al., 2018), or at “cocktail party“ frameworks as linear models that separate attended and unattended acoustics (Puvvada & Simon, 2017). A linear model like this can be mapped in a forward direction (acoustics -> cortical response), or conversely as backward model (cortical response -> acoustics) (see Bialek et al., 1991; Haufe et al., 2014; Van Eynhoven et al,. 2017). For instance at the cocktail party attention selection task, precise models of forward and backward directions, measured with EEG signals, try to unravel and even predict to whom a listener is attending to. The decoding of EEG signals, especially for the prediction of genital actions with high accuracy (a few ms), still requires better fitting models, but exhibits first fruits.

3.3.2 Ease of Language Understanding & Auditory Scene Analysis

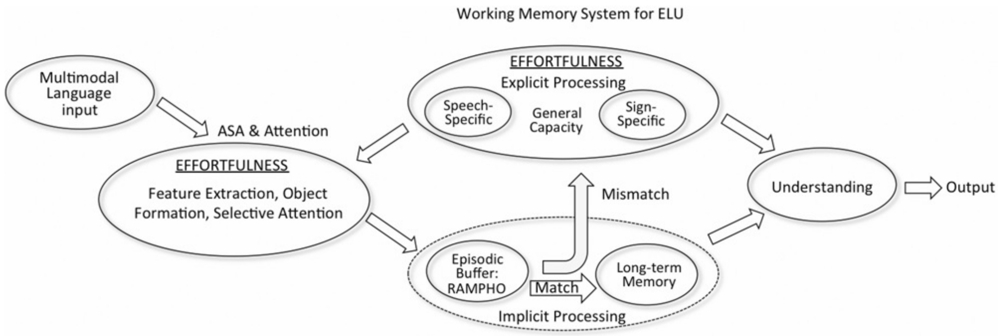
Another prominent model to lucid functional links between auditory and cognitive processing is the Ease of Language Understanding (ELU) model.



See Rönnberg et al. 2008

Models like ELU are working within a prominent framework, that includes the identification of auditory objects in space and time. For binaural cues - intramural time and intensity difference - as for temporal cues - onset, offset, duration - and pitch, the objective may be achieved in combination with auditory scene analysis (ASA). ASA displays how the difficult process of separating, grouping, amplifying, attenuating, synthesising, or making extractions within a complex environment of sounds can be realised (Wingfield 2016).

Building a hybrid of ELU and ASA, the preattentive feature of the latter gets implemented as an automatic process, happening before cognitive control.



See Rönnberg et al. 2008

With regards to the model, a better understanding of the whole process is deeply connected to awareness. In this scenario, the listener, who is in a multimodal speech input situation, could focus his attention on specific cues or speakers. The more often the listener hears the speaker, the greater the cognitive load they memorise. Through updating the implicit procession with the explicit ones, mismatches and matches are distinguished, which leads to understanding and output.

As shown here, there is a close connection between hearing and spatial awareness. Ex negativo this can be modelled by ELU and ASA for subjects that are hard of hearing. For example, if a person sneaks up behind them even though their footsteps are audible, hearing-impaired people suffer from reduced perception of the usual automatic sounds and are more likely to react with surprise. Additionally the cocktail party effect nicely illustrates how auditory capacities can spatially maneuverer through a rather chaotic spatial distributed sound complex.

3.4 Spatial Hearing

The association of auditory cues and positions in space form a set of mechanisms on which spatial hearing relies quite heavily. Tasks as locating sound sources, separation of sounds and thereby focusing attention and more general awareness, serves as notable aspects of this whole procedure. By continually applying and training these features, the auditory system can unmask sounds that otherwise remain indistinct or are just a strange noise. Furthermore this counts for moving moments as there are looming, or receding sounds. This content in particular is discussed in sec. 4. Therewith, and due to the already elaborated connections to all kinds of cognitive tasks, research in spatial hearing could reveal much more about cognitive modules, mental disorders, ability to concentrate, intelligence, etc.

3.4.1 Auditory looming bias

The central model underlying the empirical part of this research (and the Born2Hear project) is known as the auditory looming bias (ALB). ALB (see fig. 2) basically says that approaching sounds are more, quicker, or easier noticeable than receding ones. This counts for humans, but other mammals as well (e.g. mice, monkeys, etc.)
While standing at an intersection it might be relevant for survival to hear whether a car is approaching or driving away - just as prehistoric humans had to recognise whether a predator was sneaking in on them or moves away. Parts of the brain seem to process approaching noises more intensively and faster than others compared to different conditions.
Biases of any sort are evolutionary speaking a little peculiar. Instead of evolving towards a perceptual cognitive apparatus, that perceives our environment as it is, bias does something else. Whether it adds or removes ingredients of how we make sense of our worlds (internal and external), this goes beyond our senses. Of course the phenomenological phrase of investigate the world as *prima facie* and taking it perceptually most directly just as it is, seems naiv. Nevertheless our direct interaction with the world depends on our sensitive modalities and has evolved to a degree, that is inseparable from the brain and the body understood as an interactive processor. The common phrase about making sense obviously no longer makes sense when it gets this far. Moreover it emphasises sense-making as something that is not a simple and isolated process of perceptual sensing, but the vast interwoven cognitive functioning, involving thoughts, feelings and states of mind (sec. 7).

3.4.2 Sound localisation: Duplex Theory, ITD and ILD

Localisation - the ability of humans to orientate themselves in space - is to a large extent nothing other than the recognition of incoming sounds. Highly complex filters from head, pinna, and torso build the ground for the ability to localise oneself within an environment. Similar to the uniqueness of the fingerprint each ear is different (also known as an acoustic fingerprint). The shape of the head alone can have an immense influence on how long it takes for sound to travel from one ear to the next. This difference in arrival time at ear entry is recorded as the interaural time difference (ITD). Thereby a cue for the angle and the direction of the intruding sound gets calculated by the difference the sound needs to travel from left to right ear. If sound arrives directly from an azimuth of 90°, it takes the sound a little bit longer to reach the left ear (see fig. 4).[44] At azimuth 180° sound would enter directly form behind. This ITD enables the auditory circuit to process the localisation. Hence, through the difference of sound arrivals at the ears, various informations about the sound source might be identified.

Beside the ITD, there are differences in sound levels entering the ears, called intramural level differences (ILD). Rayleigh proposed the duplex theory (Rayleigh, 1907), which states that level differences are more dominant at high, than low frequencies.[45] Yet natural sounds come in all kinds of frequencies and the auditory system has to process the overlaps between ITDs and ILDs to decipher the relevant points in space.[46]

Further experiments (e.g. Woodworth 1938, Fedderson 1957) showed that at a constant distance between two ears (approx. 22-23cm) and a frequency of 1500 Hz, a maximum time delay exists when the sound arrives from exactly 90°, which is about 660 μs. That is, if the wavelength of a sound is greater than the time delay between two ears - which is the case when the frequency is lower than 1500 Hz - location cues are provided, because there is a detectable phase difference.

[44] https://sites.tufts.edu/eeseniordesignhandbook/files/2017/05/Purple_Cirone_F2.pdf

[45] Rayleigh L (1907) XII. On our perception of sound direction Philosophical Magazine 13:214–232.

[46] Jan Schnupp, Israel Nelken and Andrew King (2011). Auditory Neuroscience, MIT Press.

It must be significantly lower, otherwise the so called head shadow[47] makes it impossible for the listener to localise through ITD alone, so the ILD compensates the missing link. In between - around 1500 Hz - the phase difference is only slightly present. Consequently, the localisation process around this frequency start to become faulty.

In the horizontal plane localisation accuracy is mostly generated by ITD and ILD processing.[48] However, the elevation of the source will not cause these differences. Additionally, at the range of overtones, interferences of sound waves occur at the pinna, that is why localisation wouldn't be possible by ITDs and ILDs alone and so called HRTFs are necessary.

3.4.3 HRTFs

In order to perform precise psychophysical experiments in acoustics, one key parameter is determined by head movement-related functions (HRTFs). HRTFs are representatives or responses of sound waves entering a channel from a free field. The transfer function itself is nothing but the ratio between output and input signal spectrum as a function of frequency (free field transfer function = FFTF).

$$H(f) = \frac{Output(f)}{Input(f)}$$

The free field simulator is an anechoic chamber, in which acoustic experiments are typically made (see fig. 3). So the function modulates how the sound changes from the source to the listener. For example, a sound wave generated by loudspeakers is transmitted through the air, reverberates off the walls, is reflected by the topology of a person's head, face and ears until it finally reaches the eardrum. In general HRTFs contain spatial and temporal information according to the sound directions, but the differences from subject to subject are significant. Therefore, two types of distinctions are made: *generic*- and *personalised* HRTFs. Generic HRTFs are either cre-

[47] The head, or acoustic shadow Is a necessary given example of diffraction. Hearing (A), talking about human anatomy, requires ears (B) and ears require a head (C), so taking the inverse transitive that means without C, there wouldn't be A. Likewise the ears are flawing themselves, because of head obstructions in amplitude. Without an automatic correction of the amplitude fitting, hearing difficulties, or losses are the consequence.

[48] Blauert, J. Spatial Hearing: The Psychophysics of Human Sound Localisation: MIT Press, 1997

ated by averaging existing data from subjects, or from prefabricated dummy data sets, instead of measuring new individual sets. Another possibility would be to personalise the HRTF for an individual by comparing it to the existing database without the need for individual measurements. In any case, this is the first and most precise acoustic measurement step of many specialised experiments, because it is highly personal.

The measurement itself is literally a transfer function, i.e. the relationship between output and input is measured. The input refers to the output of the sound source, whereby the output is the input of the listener. Geometrically the sound wave spreads spherically in elevation θ, azimuth (measured clockwise) ϕ and either time or frequency. By manipulating these three parameters, sound can be simulated as if it were propagating from a particular location in space.

3.4.4 HRIRs

In order to apprehend the sound pressure - produced by the free propagating wave - at the ear drum, the concept of head-related impulse response (HRIR) is used. In fig. 5 the HRIR of the right ear is shown.[49] The brightness represents the strength. At an angle of azimuth = 90° it is strongest, whereby 270° is opposite, thus weakest. Additionally a sinusoidal shape is recognisable and the rapid changes of bright and dark bands, due to reflections of the body and the pinna in particular. Another anatomically conspicuous part is the pinna notch, the frequency of which changes with elevation.

Given the complexity of measuring three spatial variables and frequency, inverse and fast Fourier transforms (FFT) are often used to convert discrete signals between time and frequency domains. Hence the HRTF is the Fourier transform of the HRIRT and captures all important physical cues of the source localisation. This operation commonly happens at the far field, which is defined at a distance about one meter, where the turbulences are becoming noticeably weaker.

3.4.5 Measuring HRTF/HRIR

[49] https://www.ece.ucdavis.edu/cipic/spatial-sound/tutorial/hrtf/#HRTF_hor

The test person sits in an anechoic chamber so that the greatest possible isolation of the sound reflection is achieved. Microphones are inserted to the test subjects to receive sounds. Due to the arrangement of loudspeakers the movement of the subject rotating or moving loudspeakers, all angles of interest are captured and the ratios between the reference sound and the recorded sound forms the HRTF. It is also worth mentioning that the HRTFs do not capture resonating or reverberation effects.[50] It rather simulates a perfectly smooth room, without any interferences. Therefore the sounds must contain the effects of the room so that it sounds like a realistic environment.[51]

One important aspect of this arrangement is to enable the possibility of taking both into account: front and back dimensions. Other techniques, e.g. amplitude planning method, is simply operating in 2D, by using amplitude levels in stereo. Another alternative is the ambisonics recording technique, which also works in 3D but requires its own format, so it is not similarly practical to use.

Since all the basics and a lot of technical pre-requirements have been covered so far, the succeeding chapter examines the experimental part of this undertaking.

4 ALB Experiment

In this chapter I would like to explain the experimental idea, the components, the parameters, the mechanics, the instruments and the preliminary results of the listening experiment I participated in as part of my thesis. Like a walkthrough I start with an introductory part outlining the main

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50 To note: resonance is not reverb: when screaming at your computer because it doesn't do what it should, it starts to vibrate a little bit in resonance, because of the air fluctuation in density that waves at it. Reverb on the other hand, occurs when your scream would be capsulated in a room, bouncing back and forth, which prolongs the scream. This is only the case, as long as the scream gets reflected fast enough, or from a surface near enough, otherwise the screams are phase transferred and echos are created.
The specific echo threshold ranges from 20ms to several seconds, depending on various things, foremost on the typ of signal, the volume and the surface.

51 Among other examples, this gets fascinatingly demonstrated at the virtual barbershop for binaural audio.

idea, followed by an explanatory part specifying the materials and general architecture. In the remainder of the chapter, I elaborate on the individual components of the study and conclude by presenting some of the findings and discussing broader perspectives as immediate implications.

4.1 Introduction

Although there have been previous studies that have illustrated how sounds that get louder are perceived as superior compared to those that get quieter, this experiment is different. As a rule, the approach of a noise source causes a more salient perception, but so far no one has been able to clearly prove, whether the increased attention occurs due to the already anticipated approach, or just as a reaction to the increasing intensity.

Our auditory system is constantly taking in and presenting information to monitor our environment. This already includes auditory and spatial aspects and links them closely together. As such, it is an inimitable part of our survival and - less precariously put, but all too important - forms our capacity for daily survival. Along the mechanistic plasticity of our neural system, the auditory system comes not as fully evolved anthropologic craft, but needs additional learning and continues to do so through the whole span of a human lifetime, starting off as a newborn. Whether statistical or supervised learning, frequent and implicitly inattentive automation or - the latter - an attentive ability to discriminate auditory phenomena on the basis of feedback prevails remains unclear. In particular, the question of at what age, from the newborn to the young to the old adult, the weighting of the learning rate is remains unclear. Spectral shape cues combined with the auditory system and plasticity - as an ongoing learning machinery - turns this region of interest into an interdisciplinary area of research.

Earlier studies (Baumgartner, 2017) simulated the approach of noise generation by means of changes in the sound spectrum. The volume of the audio signals remained constant during the test series. Noticeable the subjects were able to recognise much better when a sound source from the sound spectrum moved in their direction than when it moved away from them. Brain activities - measured with EEG - showed also higher intensity when the source of the sound loomed closer, as when it receded. Scientifically phrased, the empirical fact that approaching sounds are more salient than receding ones is termed as auditory looming bias (ALB).

The ALB occurs effectively due to the approach and not just to changes in the tone intensity. But it also only occurs with continuous tones. If sounds interrupt in between the test subjects did not perceive the noises more intensely, even if they were simulating approaching. It appears, therefore, that constant movement of the sound source is necessary to achieve this effect.

The recent study which I joined investigates in the cortical mechanisms underlying the looming bias, transposed as connectivity analysis. According to the findings, there is a preferential top-down projection from the prefrontal cortex (PC) to the auditory cortex (AC). Next it is key to test and analyse if that specific finding can be generalised. Essentially if it holds the hypothesis under spectrally induced looms and neural correlates.

4.2 Materials

The main experiment falls into two main parts, whereby each part consists of specific measurements and the follow up is conditioned by the primary. First up, it starts with an acoustic-physiological ear measurement and secondly follows an acoustic-cognitive hearing task, while using EEG. The former can be seen as pre-study that inspects anatomical idiosyncrasies and proofs basic functional abilities. This rather sumptuous process may not be considered as a necessity, since familiar studies from other labs manage without this procedure by reverting to the established literature. Anyhow it leads to higher precision, more individuality and additionally illustrates some characteristic features the institute is known for (ISF) and where the experiment is carried out.
Depending on the date of publication and the fact that more than one experiment has been conducted, new data sets are constantly being collected, using slightly different approaches and partly combined with previous studies in this work (Baumgartner et al., 2017). In this thesis I focus on the main pinnacles of the scientific ideas and working steps that were done experimentally and computationally. By doing so I do not persist on identical coherency between description and background data of one particular publication, as it is sufficiently known and even overlaps, which is feasible for the implementation of this project.

4.2.1 Subject criteria

One important criterion for subjects participating in a hearing study is their ability to hear generally. As hearing loss is considered to occur as gradual delay, rather than some discrete threshold, it was made sure that hearing loss was not greater than 20 dB relative to normal-hearing population. This holds for a frequency of 500 Hz to 8 kHz.[52]

Arguably the first and most important resource of the whole study consists of its subjects. In total it included 33 listeners, separated in two blocks. First, paid volunteers (age 20-29 y, M = 24, SD = 3.7; 10 females, 5 males) and in experiment II 13 subjects (age 20-42 y, M = 29, SD = 5.7; 7 females, 6 males). 5 more listeners participated as subset in both experiments.

The first experiment consist of 840-, the second of 192 trials. This means that each trial represents sounds that are played to the listener. In Exp I, in 86% the spectral contrast switched, 14% stayed constant. Exp II in turn, switches happening in 100%, for every trial, so there are no constant trials. In order to learn about learning in the long run, undesired short-term learning by cues, or schemes is tried to avoid by randomising the order of the trials and reducing feedback.

4.2.2 Experiment 1: Pinna test

Prior of the auditory-cognitive task - during measurement of the EEG signals - the anatomical dimensions of the outer-ear (especially the pinna) are measured.[53] Simulation of sound source locations are used to find and define the beforehand already described HRTFs. For this trial the subjects take a seat, centred right at a half circle of 7 loudspeakers, in a semi-anechoic booth.[54] The booth itself ranges from -90° at right side of the listener, to the left side at 90°, in sampling steps of 30° each. (Acoustic Research 215 PS; amplified by Crown 1002 XTi; IAC Acoustics, single-walled, 12 ft x 13 ft) (see fig. 3). The loudspeakers levitate nearly at the level of the ears, with a radius of 1.5 m. Now the actual metric of interest are the transfer characteristics. Binaural

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[52] Informed consent was monitored by Boston University Institutional Review Board

[53] For HRTFs the filters of the Pinna are crucial, although there are other important, isotropic components that shape the HRTFs as the concha and the open ear gain. The torso and shoulders are influencing as well.

[54] Later experiments are done in a more modern anechoic chamber, consisting of 92 speakers

miniature microphones (AuPMC002; Ausim, Inc.) are insetted in the subjects ears and stabilised. Therewith the maximum length sequence (MLS) of order 15, after 20 trials, gets identified. In order to reduce noise (hereby noise could come in form of early sound reflections), foam as wave breakers is pinched to the back of the subject, on the ground and at the microphones. In order to remove further reflections the extracted impulse responses are windowed to 3 ms with 0.5-ms cons ramps and equalised by reference measurements for each loudspeaker. Additionally the recorder signals are amplified and converted with a sampling rate of 44.1 kHz (analoge-digital with Motu 24I/O).

Then, within a frequency between 1 and 16 kHz, the magnitude (dB) of the measured HRTFs were manipulated. At the same time the measured phase spectrum remained unmodified. Within a specific spectral contrast factor of C = {0, 0.51}, Gaussian white noises presented two consecutive stimuli, that are filtered by the band-limited HRTFs.
The magnitude spectrum is measured in dB and calculated as follows:

$$M_{\mathrm{c}}(f) = \mathrm{C}M_1(f) + (1 - \mathrm{C})\frac{1}{N_f}\sum_{k\in f} w'(k)\, M_1(k),$$

M (f)… magnitude spectrum in dB
N_f …frequency bins
w'… frequency weighting function

The across frequency derivative of equivalent rectangular bandwidths (ERPBs) approximates the auditory frequency resolution. Band limitation ranged between the mentioned 1- and 16 kHz filtered noise through fourth-order Butterworth filter.[55] For fade in- and outs squared sine ramps are used. A pair of stimuli faded in and out by 50 ms.

4.2.3 Experiment 2: EEG, acoustic-cognitive test

For the second part of the experiment, or in fact the second measurement, subjects are wearing a 32 scalp electrode EEG cap (Activetwo system with Activeview acquisition software, Biosemi B.V., standard 10/20 montage), while performing auditory-cognitive tasks.[56] Furthermore one vertical and two lateral electrodes are added for the record, to ease capturing eye blinks and saccades. In order to apprehend critical experimental events, real-time processing hardware (RP2.1, Tucker Davis Technologies, Inc.) marked timing and record on an additional data channel.

4.2.4 Processing of EEG data

To this day, there is not a single algorithm that solves the SNR for fuzzy data in such a way that, almost mysteriously, completely clean and well processed output data comes out of the input data. Therefore, it has a significant impact on the study as a whole, by being well prepared and drawing consequences that best fit the decisions made previously. As a rule, there are a number of conventional instructions to be followed in the proper processing of EEG data. Such a pipeline contains filter applications, re-references, rejection of artefacts, selection of window sizes, decomposition of frequency domain, or averaging. Depending on the self defined ROIs sound can turn into noise and vice-versa. The following steps illustrates how this is done for the present experiment.

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[55] Butterworth filter is a special type of signal processing filter. The frequency response should transfer to a maximally flat magnitude. So unwanted frequencies are not completely rejected, by guaranteeing uniform sensitivity for frequencies of interest. It is given in terms of the transfer function H(jω):

$$\left|H(j\omega)\right| = \frac{1}{\sqrt{1+\left(\frac{\omega}{\omega_c}\right)^{2n}}}$$

ω = angular frequency
ω_c = cutoff frequency as angular value
n = number of order in the filter (4 in this experiment)

[56] Depending on the experiment, others are done with a 64 electrodes EEG for more complex data analysis.

The leading software for this matter is the EEG toolbox, used in Matlab. This starts the process of limiting the bandwidth for signals between 0.5 and 20 Hz. Caused by a finite-impuls-response filter, in accordance with the Kaiser window design.[57] Kaiser manages to maximise the ratio of the mainlobe- to the sidelobe energy as a useful approximation, given some prolate spheroidal window (β=7.2, n=462). The already band-limited signals are epoch- and baseline corrected, up to the 200 ms foregoing event and resampled to 100 Hz. Transgressions of these epoch thresholds, like it occurs for eye channels (−800 - and 200 μV), or brain channels (−200 - and 800 μV) are removed. Further selections for choosing independent signal components for every subject (Infomax), leads to correction of eye artefacts, bad channels, or others complications and an overall rejection of almost one third of the trials for every listener (min 83 trials/condition). Matlab Fieldtrip toolbox performed a cluster-based permutation test, to evaluate the actual test statistic. Under a distribution of 500 permutations the P value was calculated by Monte Carlo estimate. At an alpha level of 0.05 a two tailed T statistic is thresholded and the maximum of the cluster-level statistic gives us evaluated the test statistic.

4.2.5 EEG Monitored auditory tests

The experiment consists of three parts: Pre-test, Exp I, Exp II (EEG-monitored). For the timing a Psychtoolbox is used, as headphone (HB7) preamps and tubephones (ER-2) for the sounds. Listeners receive stimuli with a front sound pressure that is calibrated around 75 dB and a magnitude deviation within a range of +/- 5 db.

The pre-test literally familiarises listeners with the task. For half an hour they undergo a 1—> 0 contrast switch condition test. This was to report associations with distance change, but for some cues listeners perceived instead or also a change in height. Sources of this sort were excluded from the study. Besides, listeners are asked to discriminate between approaching, receding and static auditory percepts, by selecting the corresponding source angle (1 of 3).

57

$$w_K(n) \triangleq \begin{cases} \frac{I_0\left(\beta\sqrt{1-\left(\frac{n}{M/2}\right)^2}\right)}{I_0(\beta)}, & -\frac{M-1}{2} \leq n \leq \frac{M-1}{2} \\ 0, & \text{elsewhere} \end{cases}$$

- I_0 = zeroth-order modified Bessel function
- L = window duration
- α = non-negative real number for window shape. Determines the trade-off between main-lobe width and side lobe level
- When $\beta = 0$, Kaiser window becomes a rectangular window

Exp. I continued the pre-test tasks, extended to 1 hour. It consists of 40 blocks, around 1 min each, containing 840 trials to complete (breaks of 1 min between blocks are allowed and obligatory after at least 10 blocks).
Exp. II includes discontinuous example stimuli, with an ISI of 100 ms, which allows immediate responses. With a shorter pre-test than before Exp. I, Exp. II takes about 30 min.

4.3 Results

A crucial aspect of this study is the exclusion of volume as a cause of impending (looming) bias. For this purpose, predictions are used that allow a loudness model to be developed that can be used to switch spectral contrasts. ILDs, as difference between ipsilateral and contralateral loudness, are extracted from the predictive loudness model and show that a decrease in spectral contrast is accompanied by an ILD increase in the lower two octaves and an ILD decrease in the upper two octaves.

In Exp. I listeners have to choose between 3 alternatives (approaching, receding, static), whereas in Exp. II only between 2 (approaching, receding), but for that with trials that are either occurring with instantaneous but continuous-, or discontinuous changes in spectral shape across stimulus pairs.

During Exp. I, for all listeners frequency-specific loudness changes relative to the reference spectral contrast $C = 1$ are perceived similar. At low and mid frequencies, loudness decreases when spectral contrast is decreased. Whereas loudness increases for high frequencies. This is in contrast to ILDs. Decreasing the spectral contrast ($C_1 > C_2$) shows that listeners perceive more likely as approaching and receding for increasing spectral contrasts ($C_1 < C_2$).

Response consistency, as a measure of cue salience, is different between contrast pairs (e.g.: (0 $\leftrightarrow$ 1 vs. 0 $\leftrightarrow$ 0.5 vs. 0.5 $\leftrightarrow$ 1). Larger contrast pairs had higher consistency as they targeted decreasing rather than increasing spectral contrasts. This holds for Exp. II as well. Besides, the consistency seems overall unaffected by stimulus continuity and not significant for the statistics.

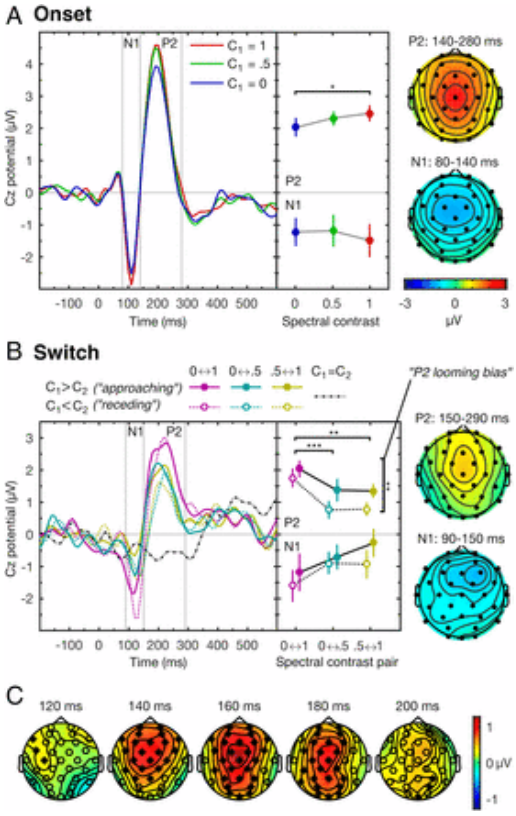

Figure 6:
ERPs by stimulus = A Onset, and stimulus switch = B and C, C_1 & C_2 are spectral contrasts.
None of switch-N1 amplitudes shows significant difference across contrast pairs. Although their magnitudes increase, with increase in contrast change.
Switch-P2 are different across contrast pairs and switch directions. Amplitudes are higher for decreasing contrast, which leads to P2 at B switch, that reflects looming bias (Baumgartner et al.).

Experimentally, looming bias comes down to ERP elicited stimuli. A frontocentral negativity (N1, Onset), followed by a central positivity (P2, Onset). For each spectral contrast, with intervals of 80-140 ms and 140 - 280ms, the amplitudes (N1, P2) are measured and averaged.

Quantifying statistical differences for increasing and decreasing contrasts, scalp distribution and timing of neural responses is performed by a permutation test. It shows a difference of 1µV (half the size of the max. Grand-average amplitude) at the central electrode (latencies around 160 ms), favouring switch directions with decreasing spectral contrast. Thus this applies for looming sounds. As a result, spatiotemporal clusters of the ERPs illustrate strong constitutional neural correlates indicating looming bias.

4.4 Discussion

In summary the study (Baumgartner et al, 2017, resp. 2021/22) illustrates looming bias for temporally continuous stimuli. Specifically looming occurs as increment of response consistency and central cortical activity. Whenever there is a time gap between the test tones, looming is no longer present. The experiments are realised in an individualised virtual environment, in which measurements of EEG and psychoacoustics are combined.

4.4.1 Looming and the brain

As described within this study, like others did before (Neuhoff, 1998, Bach et al., 2008, Stecker and Hafter 2000), perceptual bias for judging looming faster than receding appears to be neurally evident. Likewise the evolutionary point of view stresses that the observed bias has been evolved by natural selection. For an organism it is more costly to overestimate source distances (false negative error), than to underestimate approaching source distances (fasle positive error).[58] These findings (Bach et al., 2008; Baumgartner et al., 2017; Neuhoff, 2016) seem to reinforce the idea that human listeners would respond more quickly and pay secondary attention to audio-visual phenomena. As mentioned before looms - in contrast to recedes - are perceived as having faster "time to arrival" measures. This behavioural anisotropy, as noted towards increasing intensity, has also been found in infant primates (Ghazanfar et al., 2002). This means that this kind of bias appears relatively early in life. Therefore similarities of phylogenetic, in particular neural origins, are to be assumed. As it is, the auditory decoding process of sonic motion addresses fundamental questions to the origins of neural perceptual connectivity and the brains plasticity.

Looking at PAC during EEG recording of ERPs while listeners (exclusively humans in these cases) make quick judgements about whether sounds are approaching or moving away still does not show whether brain responses are caused de novo, bottom-up, or top-down, but should highlight higher activity in approaching sounds. Anyhow recent results (Bidelman et al., 2020) evidently illustrate receding signals, which are more strongly represented in the auditory system of the cortex. Nevertheless immediately hereupon the PFC overrides the sensory processing, hence higher responds according to looming are privileged.

[58] Neuhoff et al., 2009

4.4.2 Cortical areas

The cortical mechanisms that lie behind and operate in the different layers are not yet clearly understood, and some have been studied more than others. Further potential for this study undoubtedly lies in the areas that have not been considered so far but could nevertheless be considered.
In addition to PFC and PAC the inferior parietal lobe (IPL) seems to play a major role when it comes to spatial hearing in general and sound motion processing in particular. Through fMRI studies, that are often the starting point in order to localise ROIs, before continuing to unravel the time dynamics with M/EEG, the involvement of the amygdala is also highlighted. More precisely when it comes to processing the emotional meaning of auditory stimuli this becomes relevant. In both cases, external sounds (e.g. environmental soundscapes) and internal sounds (e.g. tinnitus), the emotional state can have significant direct-, or even prior effects on the activation of brain regions and thus also the measurements in general (Irwin et al. 2012).
Other regions that are involved in the auditory looming circuitry are the temporal plane, which lies at the surface of the cranium, the superior temporal sulcus (STS), also called temporoparietal junction which is more important for social interaction and the intraparietal sulcus (IPS) that would include sensorimotoric functions which are likewise not negligible given a broader perspective.

Another absolutely profound element of this study are the intensity based stimuli. As a scaling of the amplitude and variety in position the intensity induces the difference of rising, falling, or staying constant. By simulating these three components it is possible to play sounds as if they are dynamic. Yet, the variety of sound intensity alone is also considered a disturbing factor. The very thing that listeners should be able to recognise eventually turns out to be a potential confounder, because the sensitivity of response has been influenced by the strength of the stimulus (Herrmann, Augereau, & Johnsrude, 2020; Teghtsoonian, Teghtsoonian, & Canévet, 2005). This is the case for high frequencies, which the pinnae filters for incoming sounds. Thus the manipulation of spectral cues thus takes the place of pure intensity variations.

Simulated motions along the distance dimension allow countless kinds of environments, angles and situations. This is brought even further when it comes to virtual reality space. In such a scenario it becomes much more easier and complex to include, or excluded other senses, sensorimotor functions and amygdala activity. At the same time, this opens up a very wide field of possibilities for future extensions of the study. In parallel, the analytical methods must develop, which will be discussed in the following chapter.

5 Brain Connectivity Analysis

The fifth part of the thesis deals with the methods and analytic procedures of the experiment. As far as this investigation is concerned, it forms not only the centre, but also the overlapping layers of my work.

One of the most challenging problems when dealing with the brain arises from its multilayered and tremendously complex structure. So first I like to go through most common architectural classifications, which are used to make sense of the brain in order to undergo connectivity analyses. Since this classification cannot cover the entire architecture, I particularly focus on networks and graphs. Straight afterwards follows a reflection on the role of mathematical modelling in neuroscience ant its relations to connectivity. This mostly covers its current attempts, breakthroughs, limitations and difficulties. The conceptual framework will condense on three types of connectivity: structural, functional and effective, operating at micro, meso and macro levels under the guidance of fitting models, which in turn reveal different forms of connectivity. But first the architecture in use needs to be clarified.

5.1 Multilayered architecture

The brain is considered to be a conglomeration of functional units, that split into neurons at smallest scale and assemblages of neurons at larger scale. In addition these complex combined scales and regions are interacting in effective- and functionally active connections. So one reputable aspect of the complex morphology of the brain is its interconnectivity. Depending on the scale, individual neurons (microscale), that are linked by synaptic connections, reveal as microcircuits. Whereby larger populations of neurons (mesoscale) arrange themselves into networks of columns. On the even large scale (macroscale), interconnected pathways of populations and individual neurons form distinct regions in the brain.

5.2 Networks and Graphs

In various disciplines, but especially in brain research, the study of the connectivity of cortical areas is a particularly important and successful pattern for deciphering anatomical relationships. For this purpose, the anatomical regions of the brain are defined and the functional interactions between the different regions are described, such as certain cognitive processes that are active in certain time spans, statistical dependencies and causal interactions. Beside the specific processes between synaptic connections at short- and long ranges the variability is one of the major sources to express neural dynamics. As a result the plasticity of the brain, the growth rates of the connections and the development of the regions reveal functional insights.
This conception precedes the information process in the brain as almost optimal. Additionally spatial (at near and far range) and temporal correlations are understood as functionally correlated. Thus, what runs ahead of all these studies is a prior model of synchronised and functional causal activity of brain functions and cognitive dynamics.[59]

Based on the assumption that pre-formulated ROIs can be detected by means of (f)MRI or M/EEG, the results of the mathematical analysis should make correlations visible as superimposed modelling processes of data sets. As mentioned earlier, what is associated depends on the algorithm that underlies the experiments. The algorithm itself depends on the primary understanding of what is expressed by the data and what is the condition of possibility for the algorithm to find certain connections. The epistemological loop of defining findings beforehand, in order to find them, will be discussed in more detail later on.

5.2.1 Graphs

The complex topology of brain networks can be described and represented by properties of static- and dynamic graphical models (GM & DGM). In the realm of neuroscience such models are representing physical brain variables by conglomerations of parameters from the glossary of

[59] O. Sporns, Connectome, vol. 5, Scholarpedia, 2010.

graph theory. Modern attempts of increasing relevance (e.g.: B. W. Huang et al., 2018; Rosa, & Hilgetag, 2019; Pascucci, & Tourbier, 2020; Ju & Bassett, 2020) are connectome harmonics, brain gradients, graph neural fields, or Fourier modes. As a result, the brain areas and the interactions of the neurons correspond to the vertices or nodes and the associated edges, if assuming a compilation of the connectivity analysis using graphical models. The composition of edges (in this case synapses, or pathways) and vertices (individual neurons, or regions) act as so called graphs (Brandes & Erlebach, 2005). A graph is considered to be complete if it consists of N vertices and one edge between every two vertices. The spectral graph theory studies properties of graphs via the eigenvalues und eigenvectors of their associated graph matrices, which are the adjacent matrix and the graph Laplacian, but also variants of them.

5.2.2 Graph Laplacian Matrix

The Laplacian, Admittance, Kirchhoff, or also known as the discrete Laplacian, is a simple but quite important matrix formulation of a graph in use. It allows a link between discrete representations, which are represented as graphs and vector spaces, or manifolds which represent continuity. The Laplacian L is defined as:

$$L = D - A$$

D… diagonal degree Matrix
A… adjacent matrix
Thus graphical models provide the mathematical framework to describe pairwise interactions in the brain. Given the functional and effective neuronal changes, as for short- and long term changes, spatiotemporal fluctuations find fitting representations through differentiable graph modules (DGMs).

***DGMs** are graphical models that change over time. In this way, instantaneous relationships between nodes can be described while the directions of networks are estimated.*

The aim is to explore and use suitable metrics, which are capable of quantifying the *eigenmodes* of FC in the appropriate *eigenspectrum*. The geodesic path lengths between two vertices, which is always the shortest in-between, determines their functional efficacy. The degrees of correlation of the vertices, the associations of the clusters that occur, such as the motifs (subgraphs), as parameters for the positions of the vertices and edges depend on the research interest. For example uni-, or bidirectional edges between pairs of vertices within corresponding layers, can be described by differential equations, delineating development over time, or more simplistic by adjacent matrices. The rows and columns of a connectivity matrix corresponds to different regions in the brain and thereby encodes neighbourhood relations in a quantified order. Especially by investigations in small-world networks (SWNs), high efficiency at different spatial and temporal scales with a minimum of energy costs characterise features of structural, functional and effective connectivity (Guye et al., 2010).[60]

***SWNs** describe mathematical graphs in which nodes are not necessarily neighbours of one another, but most likely so, or can at least be reached by a small number of steps, within the network. Like someone would say it is a small world, context wise, here it is a small network.*

SWNs in topologies of complex brain networks share properties with many other complex systems, which indicates more general, but likewise more versatile exertions of cartographic ventures, like the connectome.

***Connectome** is the name of an ambitious neuroscientific project that seeks to trace and comprehensively map neural connections in the brain. As a goal the entire structure and all functions of the nervous system of every operating neuron and ever synapse with its dynamical interactions shall be collected and mapped.*

That is, if connectivity analysis is planned, one task is to find those nodes and edges over which extrapolation of network specifics is possible and a functional map of the brain can be created. The characteristic path length - known as the global average of all measured distances - might be of particular interest for some analyses. Multidimensional scaling, or principal component analysis (PCA) might be used for clusters transpiring through the data.

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[60] M. Guye, G. Bettus, F. Bartolomei, and P. J. Cozzone, “Graph theoretical analysis of structural and functional connectivity MRI in normal and pathological brain networks,” Magnetic Resonance Materials in Physics, Biology and Medicine, vol. 23, no. 5-6, pp. 409–421, 2010.

PCA *gives structure within a set of data by reducing the dimensions of the sampling using the direction of greatest variance. Through calculating the eigenvectors of the covariance of the data it is possible to project the significant components of the data into a more simple environment. So the complexity is reduced and it gets easier to work with.*

As it is, there exists no uniquely defined model that would always be appropriate. Nonetheless, what remains important from a statistical point of view is the design of the null hypothesis and the arrangement of parameters to form the framework, like the ones that are mentioned above.

Null-Hypothesis *claims that there is no statistical significance between variables in the hypothesis of interest.*

5.3 Connectivity Measures - Segregation and Integration

Apart from that another basic organisation pattern of the brain is characterised by segregation and integration of information (Tononi et al., 1994). In segregation, anatomical focusing seeks explanations for brain functions by localising the regions of individual neurons, neuron populations and brain regions as precisely as possible. The integration on the other hand tries to decipher how these neurons talk to each other. It is considered to be the interplay of segregation and integration that generates high diversity, but at the same time binds strong alliances in the brain complex. These two conceptual parts are based on three different types of connectivity analysis, which are explained as follows (Horowitz, 2003):

5.3.1 Anatomical-, Functional-, Effective Connectivity

Anatomical connectivity, also called **structural connectivity**, represents the interactions of white matter regions in the brain. Synaptic contacts of varying strength and effectiveness between neighbouring neurons and distant fibre tracts form the neuronal connections. Due to the plasticity of the brain, structural changes are unstable over longer periods of time such as hours or days. In contrast, anatomical connectivity remains stable over shorter periods of time, i.e. over seconds to several minutes.

In order to illustrate the tractography of the white matter in the brain, diffusion-weighted magnetic resonance imaging (DWI) is used as a special implementation of MRI. Here, the diffusion process of water molecules is imaged non-invasively and in vivo. In particular, diffusion tensor imaging (DTI), a special form of DWI, provides information about the architecture of the tissue at the microscopic level. (Taylor & Bushell, 1985).

Functional connectivity is basically a statistical concept, relying on correlations, covariance, phase locking or spectral coherence of voxel activities. Mostly all elements of a system, regardless of their anatomical linkings are included and depicted as statistical fluctuations. Hence neither the directions of correlations, nor the structures are explicitly screened. In contrast temporal dependency at around hundreds of milliseconds of neural activation patterns at brain regions are the essential part for exposing connectivity.

Effective connectivity reflects causal interaction between particular brain regions. The causal descriptions of these effects can build on spatial or structural, resp. anatomical information, or causal dependencies in time (time series analysis=TSA). [61] Effective connectivity can be considered as a combination of anatomical and functional connectivity.

Nowadays the focus in neuroscience - seeking to unravel the circuitry underlying cognition and perception - lies on functional and effective connectivity. Chapter 6 serves as an identification parade of three statistical concepts used for effective connectivity analysis: Granger Causality, Phase Transfer Entropy and Dynamical Causal Modeling.

5.4 Connectivity metrics

Before we dive into more detailed explanations of the specific connectivity analysis methods, I like to review some fairly important metrics, which are basic prerequisites in connectivity research.

When we talk about functional connectivity, we are talking about information being transmitted between regions in the cortex. Neuronal oscillations, which are expressed as action potentials,

[61] Friston, K., Moran, R., and Seth, A. K. (2013). Analysing connectivity with Granger causality and dynamic causal modelling. *Curr. Opin. Neurobiol*. 23, 172–178.

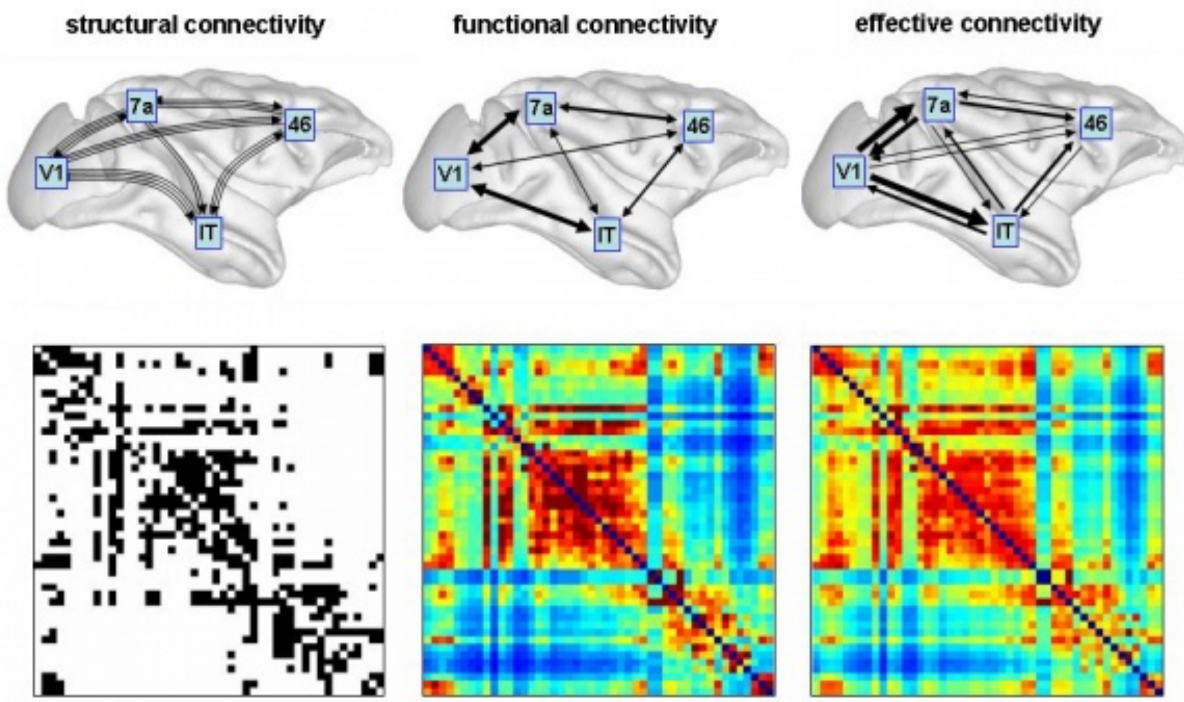

Figure 7: Modes of brain connectivity. Sketches at the top illustrate structural connectivity (fibre pathways), functional connectivity (correlations), and effective connectivity (information flow) among four brain regions in macaque cortex. Matrices at the bottom show binary structural connections (left), symmetric mutual information (middle) and non-symmetric transfer entropy (right). Data was obtained from a large-scale simulation of cortical dynamics (see Honey et al., 2007 and Sporns 2007, Scholarpedia).

cause bursts, further increase the reliability of information transmission or establish long-range synchronisation.[62] Given the hypothesis of neural oscillations, the strength, frequency, or pattern of inter-area synchronisations vary for different functions and can get described by quantitative methods, which evaluate neural synchrony in electrophysiological data. The invasive, or non-invasive collected data from context dependent, or task-free experimental designs are then processed, to provide valid interpretations of the measurements. The scientific literature furnishes beforehand a multitude of metrics, based on diligent stochastic processes like Granger causality for once and more impromptu modifications like Phase Locking Value in other cases. All with advantages and disadvantages in view of the specific context and different circumstances. Deciding what to use in which situation is crucial. Furthermore, as science is constantly confronted with new methods and discoveries, individual stochastic solutions are required more and more often. So it is a balancing act to stay at the level of the existing, well-known and proven litera-

[62] Wang, X.-J. (2010). Neurophysiological and computational principles of cortical rhythms in cognition. *Physiol. Rev.* 90

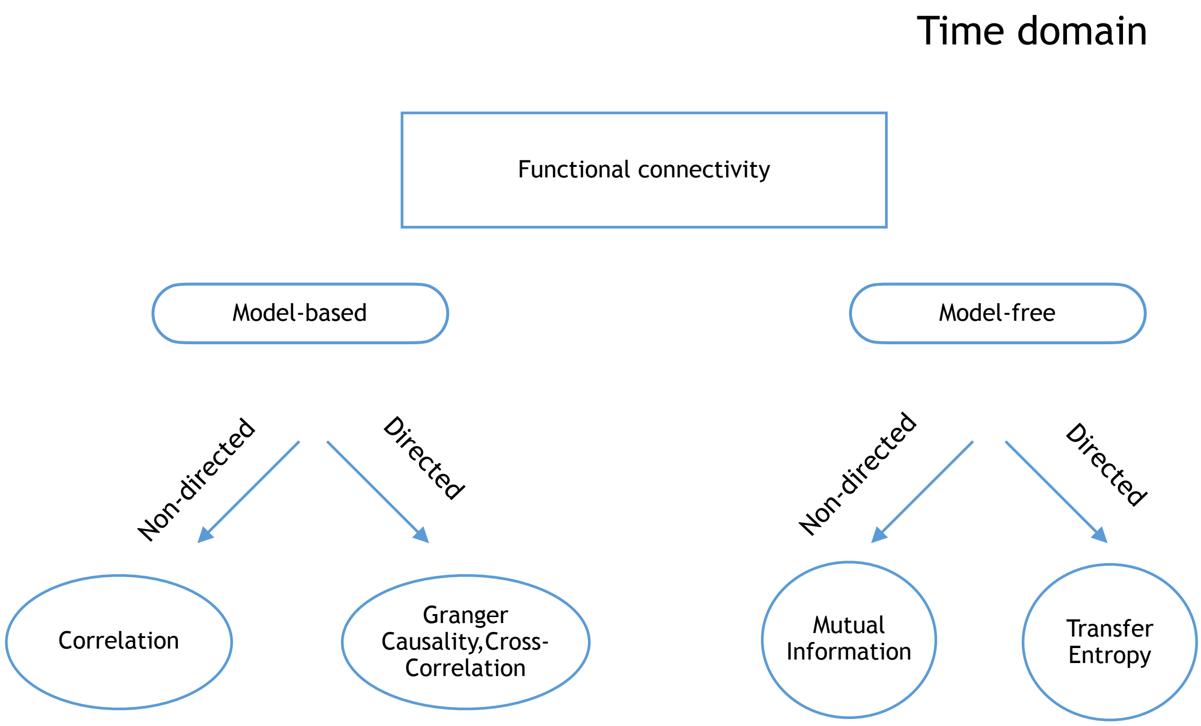

Figure 8: Schema to illustrate Model-based vs. Model-free functional connectivity methods, considering the time domain

ture, but at the same time to implement something completely different, which has never been done like this before. Given this challenge, the interpretation of the personal data collected becomes even more complicated and often over-interpreted.

5.4.1 Correlation coefficients

Functional connectivity works in the time and frequency domain. The combination of the time at which neuronal oscillations occur and in which strength, i.e. their intensity. Following this assumption, functional connectivity is divided into model-based or model-free and subdivided into undirected and directed methods of analysis (see fig. 7). Model based approaches make assumptions of linearity between the interactions of two signals. Directed or not, defines if the metrics of interaction include the direction of influence. Arguably the most simple non-directed, model based measure is the Pearson product-moment correlation coefficient (PPMCC). This method sets the ratio between the covariance of two variables and the product of their standard deviations as follows:

PPMCC: $$\rho_{X,Y} = \frac{cov(X,Y)}{\sigma_X \sigma_Y}$$

cov (X, Y) … covariance

$\sigma \frac{X}{Y} \ldots$ *standard deviation of* $\frac{X}{Y}$

As shown in this formula, an independence from the temporal structure of the data is apparent in PPMCC measurements. Otherwise, shifting two time series with respect to one another at multiple lags, a cross-correlation - here as a function of time - can be obtained.[63] Maximal correlations

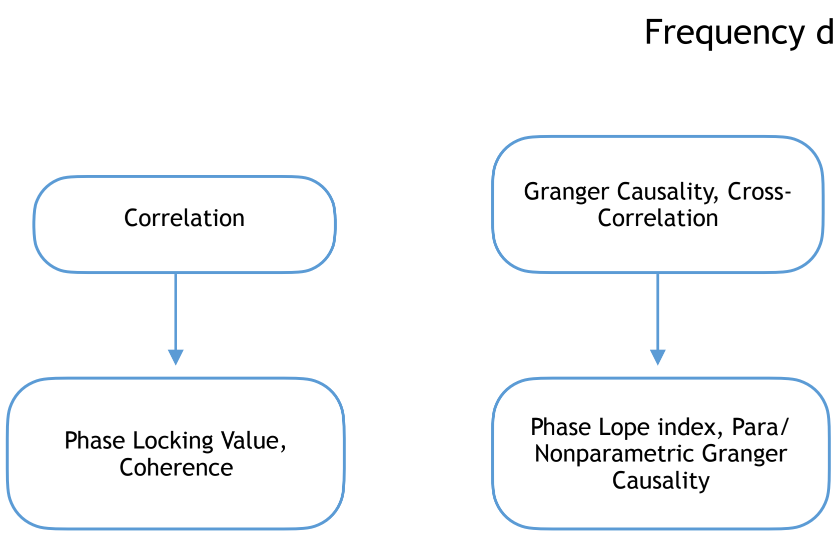

Figure 9: Correlation vs. Cross-Correlation connectivity measure in the frequency domain

are in this case reasonably informative about the effective information flow between brain areas. Such cross-correlations have proven useful to study unidirectional interactions at certain time delays.[64]

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[63] “Lags“ are used for temporal relationships as a delay in the successor. So a lag k is a fixed amount of data plotted in a time series before the event t+k occurs. In contrast, “lead“ means an acceleration of the successor activity.

[64] Alonso, J. M., Usrey, W. M., and Reid, R. C. (1996). Precisely correlated firing in cells of the lateral geniculate nucleus. *Nature* 383; Usrey, W. M., Reppas, J. B., and Reid, R. C. (1998). Paired-spike interactions and synaptic efficacy of retinal inputs to the thalamus. *Nature* 395; e.g. geniculocortical, or retina-geniculate feedforward pathways

Anyhow, the cross-correlation usually misses discrete peaks, whereby positive and negative lag values remain significant, but unclear to decipher. Additionally most cortico-cortical interactions are not un- but bidirectional. This means that the use of cross-correlations alone is not sufficient.[65]

5.5 Synchronising connectivity

Measuring the synchrony of oscillations conveniently implies the estimated amplitude and phase of a pair of signals. Geometrically this is a plot in a 2-dimensional cartesian coordination, representing complex valued numbers *(i)* either as $Ae^{(i\phi)}$, or $x + iy$. The magnitude of the vector represents the amplitude (*A)*, whereby the angle (ϕ) of the X-axis and the vector represent the phase. This gets combined with additional signals and spectrally cross-correlated by multiplication of the signals with the complex conjugate, of the other signals. As a result we have two or more signals plotted by difference in phase.

In order to measure synchrony, the distribution of phase differences is quantified and correlated as probability distribution. This can be achieved by normalising all vectors from head to tail and take their weighted sum. A significant non-zero value of two cross observations counts for some consistency as they add up, where a zero or near-zero value represents a shift. This relationship can be illustrated quite simply and clearly shows the synchronisation within a data set.

5.5.1 Coherence coefficient

Another approach to quantify synchrony is the coherence coefficient. That is a normalised quantity bounded by 0 and 1. Between a pair of signals, the squared value as a function of frequency represents the variance of one signal, which can be explained by the squared value of the time domain of the other signal. However this approach may lead to ambiguous interpretations, be-

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65 Another alternative to Pearson would be Spearman. Instead of proportional correlations, Spearman builds on ranking driven correlations. That means the rate of change for two variables are not necessarily equal.

cause of larger phase delays in the frequency domain.[66] Therefore a particular range as a fixed time delay between two signals offers a phase difference that can get interpreted instead. The slope of the phase difference is further used as a function representing the coherence within the region of interest.[67]
However, it is argued that the technique of normalising individual observations reflects artificial phase synchronisation rather than the coherence that lies in the data. Phase locking values (PLV) support processing of the data, so that amplitude correlations between measured signals can be detected. The same applies if the frequencies were still very different, so that even perfectly correlated amplitude functions would be highly artificial and worthless.

Another application of the metric is to quantify the distributions of phase differences across multiple observations. Such distribution methods (PLI=phase shift index, PPC=pairwise phase consistency) are calculated from all pairwise differences, in contrast to PLV, where a vector averages the relative phases. By computing pairwise differences, individual clusters that occur in the data can be detected. Other than PLI, PPC works unbiased, so the number of trials make no difference for the expected PPC value, which has its ad- and disadvantages, depending on the available data. This interpretational difficulties are fairly similar to the sample size problem, or the ongoing SNR controversy.

5.5.2 Phase Slope Index

For changing phases, as it is the case for unidirectional interactions, the phase slope index is used. So this means working with a modified bandwidth parameter that clarifies the frequency range, i.e. the change in phase difference. Thereby the complex valued coherency computes and quantifies the change in phase across the frequencies of some signals. If the index deviates from zero, there is significant coherence.

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[66] Phase difference works as circular modulo 360°. If the discrepancy is larger it gets impossible to transfer.

[67] Friston, K. J., Bastos, A., Litvak, V., Stephan, K. E., Fries, P., and Moran, R. J. (2012). DCM for complex-valued data: cross-spectra, coherence and phase-delays. *Neuroimage* 59

By using the complex value, the imaginary part of the coherence is projected onto the y-axis (imaginary axis).[68]

5.5.3 Spike-Field Analysis

One way to go beyond pairwise metrics for connectivity analysis is to use partial coherence.[69] To eliminate indirect influences on the estimates and inherent data processing problems, i.e. problems that only occur due to the processing method used. Using a complete cross-spectral density matrix, a partial cross-spectrum can be determined. The spikes of individual neurons, which are basically induced action potentials, and the electromagnetic fields that occur while patients are performing a certain task can be visualised by the so-called spike field analysis..

So far, some of the most important metrics for connectivity analysis have been mentioned here, now I would like to continue the identification parade and start with Granger causality.

6 Models of neural dynamics

Functional and effective connectivity are linked by overlapping areas in their methodology, but at the same time clearly distinguishable from each other. The first deals with statistical dependence between at least two or more variables, while the second aims to find underlying physical mechanisms that are elucidated by data analysis. In other words, functional connectivity looks for correlations in brain activity, while effective connectivity refers to patterns of causal interactions.

Let's take an example, when two parts of the brain process acoustic information, they share the process and in response both parts of the brain should light up. What is still missing, however, is the direct influence or effect that one part of the brain has on another and vice versa. Effective

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[68] García Domínguez, L., Stieben, J., Pérez Velázquez, J. L., and Shanker, S. (2013). The imaginary part of coherency in autism: differences in cortical functional connectivity in preschool children.

[69] Rosenberg, J. R., Halliday, D. M., Breeze, P., and Conway, B. A. (1998). Identification of patterns of neuronal connectivity–partial spectra, partial coherence, and neuronal interactions. *J. Neurosci. Methods* 83

connectivity is exactly what direct causal interactions are engineered for. Howsoever, in order to determine the time- and frequency-dependent interactions, a specific model is required. Consequently, effective connectivity analysis is also referred to as *“model fitting exercise“* (Friston, 2008). To make sense of the data, the most promising model that best fits the data, i.e. makes accurate predictions, is of highest interest.

6.1 Granger Causality

Given a range of applications, but particularly when it comes to connectivity, the interest is in understanding the interactions between datasets. Irrespective of the type of interaction, causality and prognosis play an important role, indeed so important that both even merge into each other as described in brief.

Take $H_{<t}$ as all relevant information that lies historically to the time *(t-1)* and the optimal prediction of x_t given $H_{<t}$ as $P(x_t | H_{<}t)$, y is causal for x if for the variances holds the following:

$$var[x_t - P(x_t | H_{<t})] < var[x_t - P(x_t | H_{<t} / y_{<t})]$$

That expression tells us that $H_{<t} / y_{<t}$ excludes all values $y_{<t}$ from the history and the variance of the optimal prediction error is reduced by including values $y_{<t}$. Therefore it follows that the inclusion of past values of y improve the predictability of x and y is *causal* to x. Causality is referred to as something that is ordered in time and the predictability is interwoven with the mechanistic influence of which a cause has on an effect. This indeed led to the specified term G-causal, instead of causal in a more classical sense.

Thereby Granger causality (GC) evolved to an important representative of functional connectivity in the field of modelling. It serves as a statistical paradigm for identifying directed functional interactions and is defined for time and frequency domains (see sec. 6.1, model of domains). In fact, GC evidences can occur in situations where random variations of variables can be modelled, and they are exclusively useful in these situations. As long as this is the case, however, juxtapositions are formed on the basis of model errors.

Timeline of GC

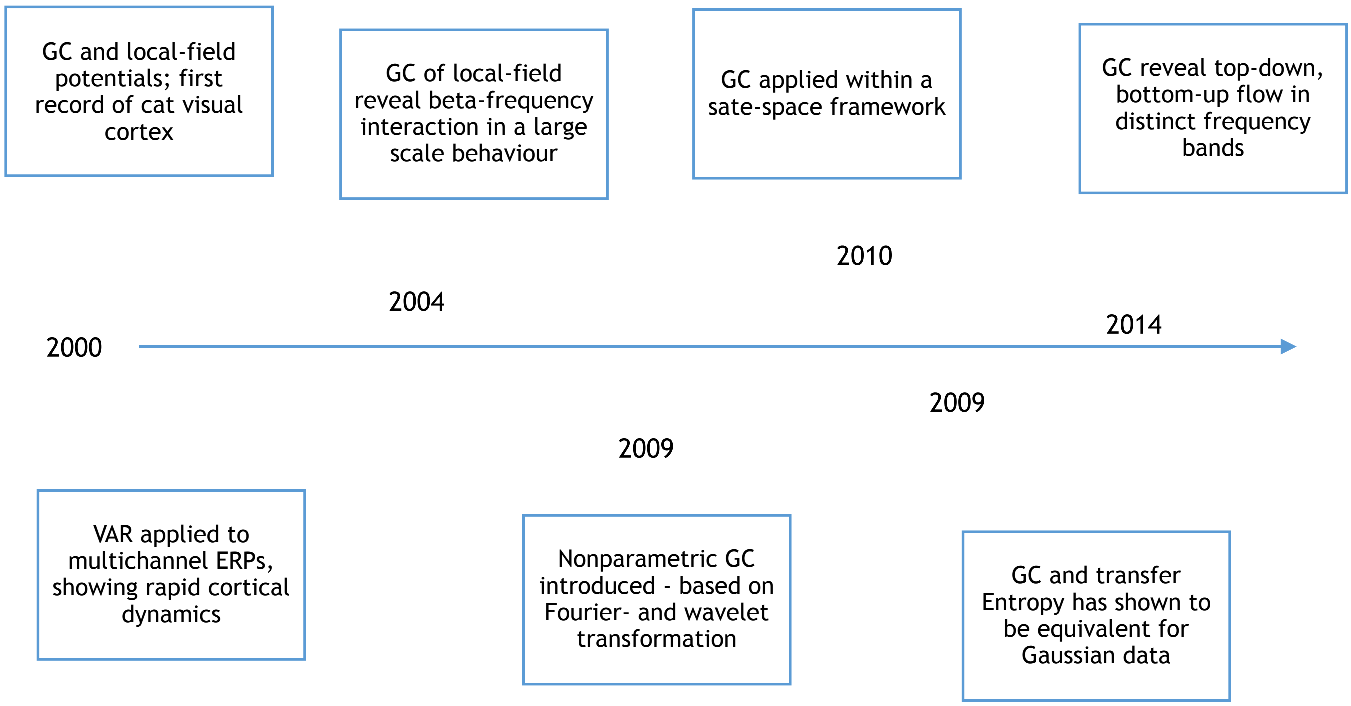

Figure 10: GC from 2000 - 2014

Originally developed in the field of econometrics, GC has found applications in a broader areas, particularly in neuroscience. For decades the main ways of studying the effects of one part of the cortex on another have been either to stimulate- or lesion the first part and investigate the outcome in the second. Focusing on predicting ongoing processes in one part of that in another entails a fundamentally different approach to identifying connectivity in neuroscience. The term G-causality is itself a predictive notion, whereby causes precede and should predict their effects. Earlier definitions followed the ideas of Wiener (1956):

A signal x causes a signal y if the past of x helps in the prediction of y

Granger (1969) took Wieners concept, with the aim to end the long lasting discussion about causality and to adept it to econometrics.[70]

[70] Granger CWJ (1969) Investigating causal relations by econometric models and cross-spectral methods. Econometrica 37

On the other hand something fails to G-cause if it is of no help forecasting the course of the conjuncted other variable. So if the predictive error can get reduced by including an additional variable. It is again important to mention that Granger is nothing else than a statistical tool, trying to reduce forecasting error by using it. Thereby the data is stationary and cannot entail theoretical models that are functioning behind the forecasting process. At least in the context of a vector autoregressive model (VAR).

The VAR model is a system of simple mathematical models, representing the relationships between multiple variables. Thus current observations of a variable are related with past observations of itself, but also with other variables. The variables are then vector stochastic processes of some particular time series. Such a time series model collects data from different points in time and lays the ground for further operations like Granger.

In order to use this idea of predictability in the field of causality, the quality of a given event must be quantified. The VAR model helps to optimise the quantification process by finding weights that minimise the estimation error.
So causality in the Wiener-Granger sense is therefore based on the statistical predictability of a time series derived from knowledge of one or more other time series. This leads to some kind of weak, but operational form of the prior definitions of GC. The idea of improving predictions is generalised by encoding it into conditional dependency, or independency.

Originally Granger (Granger, 1969) based this theory on a unique linear model:

$$A^0 x_t = \sum_{k=1}^{d} A^k x_{t-k} + e_t$$

A^d are *n x n* lag matrices of finite or infinite order (also lag). e_t stands for the error term that can have a diagonal or non-diagonal covariance matrix. So unless A^0 is diagonal, this is a simple not identifiable causal model. In contrast to instantaneous casual effects (when A^0 has nonzero off-diagonal values), this general form corresponds to the *structural* (S)VAR model and is identifiable (Kilian & Lütkepohl, 2017). But in order to establish a useful framework for the (S)VAR model, assumptions are needed:

- *Linearity* - real world processes are non-linear, but casually effecting variables within this data model need to be
- *Discrete-time* - if the data rate is slower or irregular, causality may be violated
- *Known lag* - history of data needs a known, linear order
- *Stationarity* - processes are time-invariant, resp. not evolving
- *Perfectly observed* - variables that are observed, need to be without measurement error
- *Complete system* - there are no hidden parameters in the data, alle relevant variables of the system are completely known
- *Continuous-valued series* - given the model the observations are assumed to be continuous valued, instead of discrete-valued

Mathematically this is possible for a system containing at least two variables X and Y (bivariant system) that early approaches of GC much focused on. Using the basics of a VAR (4) model we have:

$$x_t = c_1 + \sum_{i=1}^{4} \alpha_{1,i} y_{t-i} + \sum_{i=1}^{4} \beta_{1,i} x_{t-i} + \epsilon_{x,t}$$

$$y_t = c_2 + \sum_{i=1}^{4} \alpha_{2,i} y_{t-i} + \sum_{i=1}^{4} \beta_{2,i} x_{t-i} + \epsilon_{y,t}$$

This shows a bivariate SVAR model (n=2) and when A^0 is diagonal GC corresponds to nonzero entries in the autoregressive coefficients. In practice, at least two VAR models are compared at the beginning of a GC analysis like this one. Technically the GC has a magnitude composed of the variance ratio and the prediction error, for reduced and full regression. Beforehand a full VAR model estimates the error between variables and enables predictions. Cutting off the low potent variables, a second, reduced VAR model is estimated and the prediction error shrinks. If the prediction errors for the full regression are smaller than for the first regression alone, a G-cause is found. [71]

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[71] Barnett L, Barrett AB, Seth AK (2009) Granger causality and transfer entropy are equivalent for Gaussian variables. Phys Rev Lett 103

Next, a Wald test[72] can be performed to find out which parameters are statistically significant and which are not.[73] Doing so, a model with X alone, that excludes Y and one with Y alone, excluding X is compared to implicate a X^2 sampling distribution, as n approaches infinity. The null hypothesis of the excluded models suggest that the variables in question can be removed, without significant changes in the model.[74] So if the Wald test shows, the parameters that could have explanatory influence are zero, they can be removed from the model. This, as a consequence simplifies the whole process.[75]

6.1.2 Multi varied GC

The causal interaction in a bivariate system is quite easy to see and fairly limited. It becomes more difficult, but also exciting and expressive when multivariate systems are involved. Over time many different versions and derivations of the original GC idea have developed. Most are of higher complexity, involve more parameters and variables, and drop some or even multiple of assumptions listed above. For example, the need for linearity is eliminated in order to be closer to the real world, stationarity is eliminated insofar as processes can continue to change, or the number of lags is no longer limited. In such scenarios, it is no longer trivial to claim that X is the cause of Y, since Y could also be caused by the causes of Z or other variables. This can be modeled in a VAR(4) system for x, y and z:

$$x_t = c_1 + \sum_{i=1}^{4} \alpha_{1,i} y_{t-i} + \sum_{i=1}^{4} \beta_{1,i} x_{t-i} + \sum_{i=1}^{4} \gamma_{1,i} z_{t-i} + \epsilon_{x,t}$$

$$y_t = c_2 + \sum_{i=1}^{4} \alpha_{2,i} y_{t-i} + \sum_{i=1}^{4} \beta_{2,i} x_{t-i} + \sum_{i=1}^{4} \gamma_{2,i} z_{t-i} + \epsilon_{y,t}$$

---

72 $W_T = \frac{[\hat{\theta} - \theta_0]^2}{1/I_n(\hat{\theta})} = I_n(\hat{\theta})\,[\hat{\theta} - \theta_0]^2$, $\hat{\Theta}$ = max. Likelihood Estimator, $I_n(\hat{\theta})$: expected Fisher Information

73 Another alternative would be the *F-test*: testing the *full mode*l, including all past values of x and y and subtract it from the reduced model that contains values of x alone.

74 Agresti A. (1990) Categorical Data Analysis. John Wiley and Sons, New York.

75 This is extremely useful for large sample sizes, where it is roughly equivalent to t-test and Lagrange multiplier test. For small sample sizes (<30), Likelihood ratio tests are preferred. (Agresti, 1990)

$$z_t = c_2 + \sum_{i=1}^{4} \alpha_{3,i} y_{t-i} + \sum_{i=1}^{4} \beta_{3,i} x_{t-i} + \sum_{i=1}^{4} \gamma_{3,i} z_{t-i} + \epsilon_{z,t}$$

Consequently, instead of chaining up all possible causes, a group of potential influences can be collected, e.g. in the form of O(…). Since all possible causes are contained in a set, it is functionally easier to check whether X is the cause of O.[76]
Another variation of illustration would offer the Network GC for identifying relationships among a large set of variables, which are compactly represented as a graph (Eichler, 2012).

This also connects with accounts that try to investigate in the relationship between exogenous and endogenous variables. One approach could be to integrate factors in the model, so called factor-augmented VAR (FAVAR), that are representatives of both. Or else by using different kinds of tuning parameters that can control the nonzero entries element-wise, as high-dimensional VARs on the one hand, or on the other hand through Bayesian estimates of the priors. The latter can be used as an extension and induce group-level shrinkage.

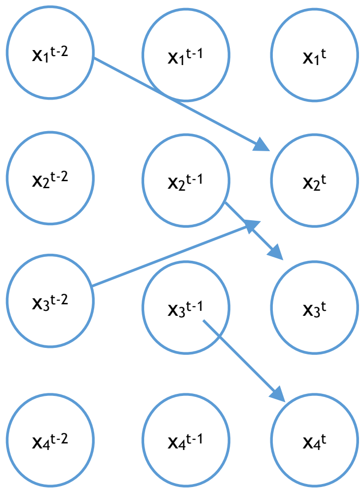

Figure 11: graphical model, replicating variables over time

Therefore, larger sets of variables can be used, and automatic lag selection, non-stationarity or non-continuous aberrations explain this rather flexible range of GC.

6.1.3 Properties of GC

Finally, summed up a short list of classical Granger properties that are advantageous when using stationary data:

[76] Other types of Granger causality tests: Toda & Yamamotot (1995), Single Fourier Frequency Granger Causality (Enders & Jones, 2019), Single Fourier Frequency Today & Yamamoto (Nazlioglu et all., 2019), Cumulative Fourier frequency Granger Causality (Enders & Jones, 2019), Cumulative Fourier frequency Toda & Yamamoto (2019)

- means and variances of the variables are stable over time
- GC is invariant under rescaling of variables
- Easy to compute (e.g. VAR)
- No underlying a priori assumptions about physical mechanisms are necessary
- Follows asymptotically X^2 distribution. Statistical significance can be tested without resampling the data, without "Münchausen-trick" (bootstrapping)

6.1.4 Limitations

Depending on the specific choice of the GC relation and the associated model, there are many to almost no limitations. Although in the latter case it is difficult to speak of GC in the classical sense, therefore we will stay closer to the classical or semi-classical applications of GC. As with most simple models, simplicity can prove useful up to a point, but loses its advantages when it comes to more complex data sets. Granger almost only models linear interactions, although non-linearity can sometimes be approximated, but solely if the data set remains to be small enough. Otherwise severely biases or high variance lead to spurious and redundant shortcomings. In its simple form it is theoretically practical, but turn out to be much harder to use in real world practice. Advanced methods such as the radial basis function (Ancona et al. 2004) and locally linear neighbourhoods (Freiwald et al. 1999) attempt non-linear regressions but are less applicable.

Additionally the VAR model that is used in GC analysis can be extended with a VARMA model, which ads a moving average component and makes it even more flexible to work with, e.g. in a state-space framework or under more noisy circumstances.

Apart from that, the GC signals are covariance stable. Ideas for analysing non-stationary data like the windowing technique (Hesse et al. 2003), or trial-by-trial (Ding et al. 2000) are approaches that divide non-stationarity into small stationary parts. Hence this can maximally be an asymptotic approximation to a non-stationary GC analysis.

Although GC can be considered as a powerful theoretical framework to study influences between signals mathematically, directed information theory provides the measures to test theoretical assertions practically. Granger is justified as approximation to phase transfer entropy, which follows next.[77] [78]

6.2 Phase Transfer Entropy

In contrast to strongly model-based methods like GC, phase transfer entropy (PTE) works completely model-free. It is therefore not dependent on previous data that is assumed when the data is created. Anyhow, PTE is a measure of directed connectivity among neural oscillations. If a signal X has a casual influence on Y, it can be separated if Y is conditioned on its own past alone, or on the past of X as well. By using the term entropy, this can also be formulated in such a way that the entropy of the present Y decreases when knowledge about X and its past is added. Following this assumption another way to describe PTE is to define it as a reduction of necessary information to decipher Y. Especially when M/EEG data sets are available without prior assumptions for data generation, PTE can be an effective tool.

As mentioned earlier, GC is considered an approximation of TE. However, TE is not synonymous with PTE. The latter literally filters between phase time-series. Thus TE is sometimes also called real-valued TE, without additional phase filtering. Comparisons of these two showed that PTE is computationally more efficient and highly robust to nuisance parameters.[79] Furthermore, TE usually gets confused when it comes to bidirectional frequency band interactions, which PTE, on the other hand, is able to decode accurately.

Within the realm of statistics, uncertainty gets substituted as Shannons Entropy H:

$$H(X) = -\sum_{i=1}^{n} P(x_i)\ log\ P(x_i)$$ [80]

[77] For Gaussian variables (normal distribution) these two are overlapping

[78] Barnett L, Barrett AB, Seth AK (2009) Granger causality and transfer entropy are equivalent for Gaussian variables. Phys Rev Lett 103

[79] The nuisance parameter can possibly be every parameter in the data, that is not directly of interest, but still necessarily taken into account.

[80] Shannon, Claude E. (July 1948). "A Mathematical Theory of Communication". *Bell System Technical Journal*. 27

X… *random variable*
$x_1, \ldots, x_n$… *possible outcomes*
$P(x)$… *probability of x*
log… base(2) = digits, base(10) = dits, base e = natural units

The possible outcomes $x_1,\ldots,x_n$ of a discrete random process X (like flipping a coin, or rolling dice), works with an inherent probability of $P(x_1),\ldots,P(x_n)$. Taking the sum of the processed variables gives a value from minimum surprise of 0, to maximum surprise of 1. This is then considered as the expected value of the system and the utterance of the uncertainty within.

The equation thus expresses the average missing information in a random source. However, instead of expressing Shannon entropy (H) only for a causal evolution from X to Y, PTE takes into account the past of Y (Y(t')) and the past of X (X(t')) and Y (Y(t')).[81] Which in turn leads to the TE equation:

$$\mathrm{TE}_{X\text{->}Y} = H\,(Y_t \,/\, Y_{t-1:t-L}) - H\,(Y_t \,/\, Y_{t-1:t-L}, X_{t-1:t-L})$$ [82]

And for directed phase transfer, it is suitable for large-scale directed connectivity analyses, including time series:

$$\mathrm{PTE}_{X\to Y} = H\Big(\theta_y(t), \theta_y(t')\Big) + H\Big(\theta_y(t'), \theta_x(t')\Big) - H\Big(\theta_y(t')\Big) - H\Big(\theta_y(t), \theta_y(t'), \theta_x(t')\Big)$$

$\theta_{x/y}(t)$ … *instantaneous phase time-series* & $\theta_{x/y}(t')$ … *past states*

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[81] Lobier u. a., „Phase transfer entropy: A novel phase-based measure for directed connectivity in networks coupled by oscillatory interactions“. NeuroImage, 2014

[82] This expression implicates, that the PTE won't be negative. Since uncertainty of the present Y cannot get increased, PTE can maximally become 0. Additionally there is no extreme value, or upper bound, neither values that could represent significant data limits, nor absolute connectivity.

It is easy to see that different phases are included (t), so that the handling of the whole data set becomes more robust and computationally efficient to realistic amounts of noise. As a consequence, the phase based transfer entropy equation is suitable connectivity analyses for larger frequency band and complex directed interactions. Based on these two equations and the factors taken into account, it is easy to manage whether TE or PTE is preferable in order to detect directional interaction patterns in the data.

6.2.1 Limitations

Studies (e.g. Ursino et al. 2020) have tested PTE and recognised this method as a reliable estimate of connectivity, but exclusively for epoch lengths of less than 10s and exclusively for linear neuronal regions. Multivariate networks may lead to counterfeit statistical measures in significance, even if there is an absence of a true connection.

In general, non-linear connections and information transfers between two ROIs, even if there is a strong real connection, can be weak, noisy or faulty. This counts not only for bivariate but also multivariate PTE (see Garcia-Medina and Hernandez, 2020). As an effect, changes during cognitive tasks, likewise changing brain conditions, might reflect different information transmissions, rather than changes in the connecting network.

6.3 Dynamic causal modelling

The basic idea behind DCM is to create a tool that is able to model cortical interactions between regions or nodes that are active in the brain. So this is not only about stochastic interactions in data sets, but physical mechanisms, that open up the causal architecture of dynamical systems, like the cortex. The guiding idea is based on the assumption of functional segregation or specialisation of brain activity on the one hand and the possibility of observing these functions (M/EEG, fMRI etc.), leading to functional integration on the other. Hence it is all about the dynamics of fluctuations of brain regions, that are causing brain activity in various detectable regions. Therefore it is named and self-evidently holds the term dynamic causal modelling. In the true sense of the word, a model of causal modelling is of interest to explain functional couplings that combine functional segregation and integration.

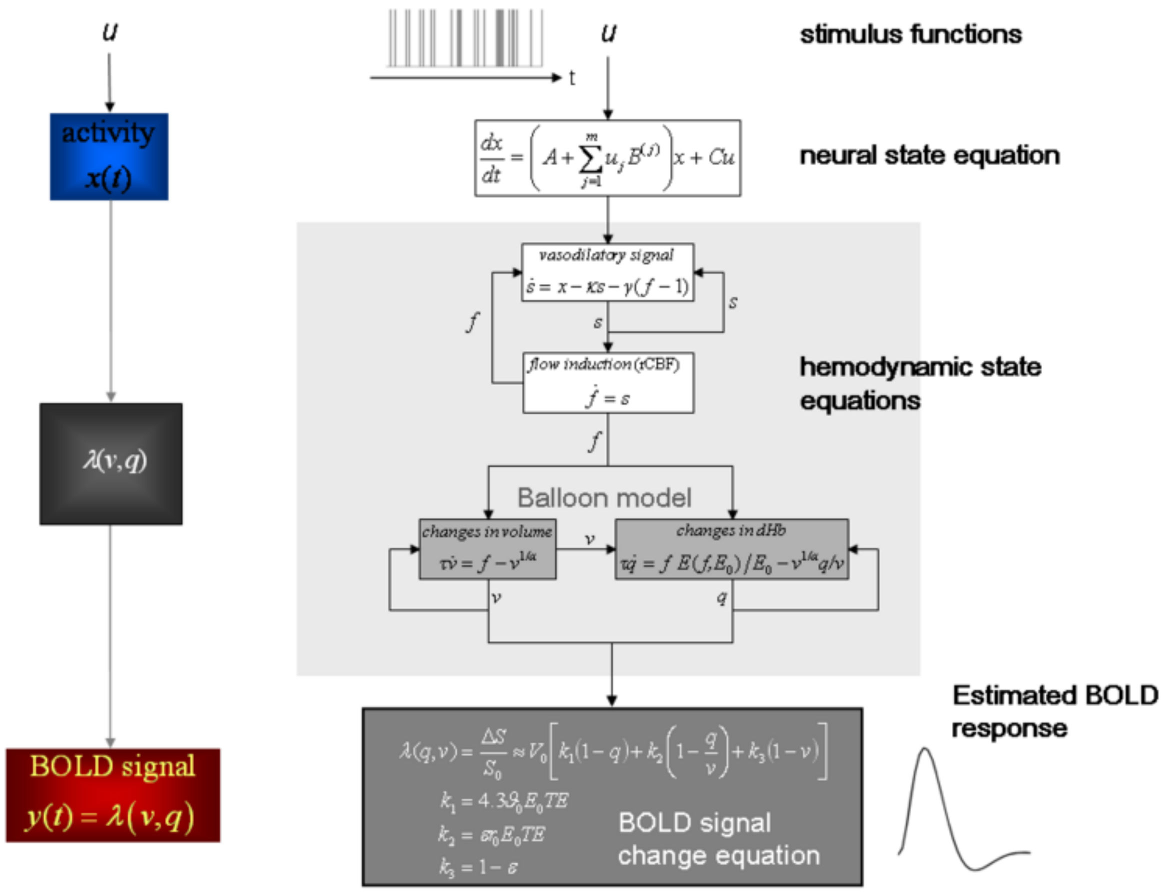

Figure 12 : "Schematic of the hemodynamic model used by DCM for fMRI. Neuronal activity induces a vasodilatory and activity-dependent signal s that increases blood flow f. Blood flow causes changes in volume and deoxyhemoglobin (v and q). These two hemodynamic states enter an output nonlinearity, which results in a predicted BOLD response y. In recent versions, this model has six hemodynamic parameters (Stephan et al., 2007c): the rate constant of the vasodilatory signal decay (κ), the rate constant for auto-regulatory feedbackby blood flow (γ), transit time (τ), Grubb's vessel stifness exponent (α), capillary resting net oxygen extraction (E0), and ratio of intra-extravascular BOLD signal (ϵ).E is the oxygen extraction function. This figure encodes graphically the transformation from neuronal states to hemodynamic responses; adapted from (Friston et al., 2003)."

Technically speaking, the combination of segregation and integration is a state space analysis, which is the same as for the weather, economical markets, or other similar kinds of stochastic systems. The state-equation itself is based on neurobiological responses and an observer equation, represented by a model. By integrating the responses through the model, a predictive measurement is generated. The dynamics of the integration are formulated as differential equations of matrices, that are representers of averaged connectivity and modulations in connectivity due to the experimental input. So the vectorised data (since it is physical brain data it has topological components) and associated likelihood corresponds to a convolution of input and response. Free parameters (typically θ) are used to minimise the discrepancy between prediction and observation, which is also known as Variational Free Energy. Additionally the predictions are specified by a prior density relation, according to Bayes' rule (Friston et al, 2003).

6.3.1 Major components

The dynamics are in fact differentials.[83] So the equations describe the hidden dynamics at a level of detail constrained by the measurement. In order to declare structural control about the complex mechanism, causality refers within this context to a perturbation of the equilibrium of the neural dynamics, which are causally propagating through networks to other regions of the brain. Since we are dealing with uncertainties when dealing with the results of differentials describing temporal developments that extend into the future, a consistent quantification of the probability distribution is given by Bayesian inference. This can be interpreted as an additional tool that introduces constraints that ensure robust parameter estimation and likewise allows to draw conclusions from observed data. However, based on the conclusions drawn, uncertainties can be updated and thus more evidence and higher flexibility can be provided. Yet it should be mentioned that this approach is also being criticised as biased or artificial, because it shall be prior introduced into data processing to play into the hands of scientists. Against these allegations it should be accentuated that the posterior distribution is provided, which is stronger determined by the data, not the scientist. Notwithstanding the scientist is still the designer and therefore to some extend prior to the posterior, as for the inverse modelling attempt. But this argument wouldn't hold, compared to the biased effects of other influences. Moreover inference can only occur for prior - post differences and if this is the case, the rate of change as "new" data speaks for itself, as demonstrated by the model evidence. But the fact remains that the prior has a dramatic impact on the objective aims. Therefore priors are specified by having a global minimum and are defined under Gaussian assumption. The global minimum raises the robustness of the objectivity of the function und Gaussian attaches the prior parameters to mean and variance. The mean equals the expectations and the variance the information which was prior available. Hence if there were precise prior information, the variance is small and the distribution is tight.[84]

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[83] Dependent on the design of the experiment the evoked responses of EEG are not always precisely located in time. E.g. in dream research under sleep conditions, or psychiatrical studies, it may happen that one has to estimate the onset and duration of inputs, as these are unknown. A steady-state paradigm is applied, apparently dealt with nonlinear differential equations that initiates a starting situation with white noise input, that is distributed over a spectrum, but can then be shaped via a transfer function. Thus, the unknown, but real inputs are manipulated and specified in DCM parameters and then tested using the inference hypothesis. More precise examples are applied by Moran et al, 2007.

[84] Comparatively, to see parts of this description: Jansen & Rit 1995, David et al 2006

Four major components of DCM can be listed as follows:

1. The model is formulated in terms of stochastic or ordinary differential equations

2. This model transforms neural activity to a hemodynamic, or electromagnetic response

3. A set of in-built biological plausible parameters are as prior parameters implemented

4. Optimising the model and the parameters of the observed data by Bayesian inversion

6.3.2 DCM and fMRI

Although fMRI scanning plays a minor role in this thesis, I start with a short explanation of the applications of DCM, using fMRI, as this is the most common and suited combination (fMRI + DCM). Anyhow, afterwards, I go into more detail about DCM applications with ERPs using EEG.

Mathematically and for fMRI experiments, DCM boils down to the so called Balloon Model (fig. 11). That is the combination of the neural state equation and the hemodynamic state equation, as the BOLD[85] signal change equation. This is necessary, because the cognitive system at its underlying neuronal level remains not directly accessible for fMRI. So the neural dynamics are transformed into area specific BOLD signals. This leads from a neural state equation, to the hemodynamic and finally an estimated BOLD response.

As it is only incidental to the connectivity here, but valuable for a broader understanding, I would like to briefly discuss what I consider to be the most important mathematical steps leading to the BOLD result. In addition, there is a figure, mostly found in the literature, that gives a more detailed insight (fig. 11).

6.3.4 Neural state equation

State equations are ordinarily first-order differentials, that are normally derived from three neuronal subpopulations, which are operating similarly as linear damped oscillators. The subpopula-

[85] =blood oxygenation level dependent

tions consist of excitatory pyramidal as outputs and the inputs, from inhibitory and excitatory interneurons (fig. 12).

$$\dot{x} = f(x, u, \theta) = Ax + \sum_{j=1}^{m} u_j B^{(j)} x + Cu$$

x…neural states of sources
$\dot{x}$…dx/dt…derivative of x
u…exogenous input
θ…prior assumption
A, B, C…matrix for fixed or modulated connectivity, resp. input parameter

6.3.5 Hemodynamic state equation:

$$\text{CO} = \frac{(MAP - RAP)}{TPR}$$

CO…cardiac output (in L/min)
MAP…mean arterial pressure (in mmHg), the average pressure of blood as it leaves the heart
RAP…right atrial pressure (in mmHg), the average pressure of blood as it returns to the heart
*TPR...total peripheral resistance (in mmHg * min/L)*

And additionally the velocity of the blood flow (v) is calculated:

$$v = \frac{Q}{A}$$

Saying that the velocity of the blood flow, that streams across a circulatory system, is determined by the area of the cross section it flows through.

6.3.6 BOLD signal

The predicted BOLD response shrinks down to the following expression:

y(t) = λ (v,q)

λ (v,q)… changes in volume and deoxyhemoglobin due to blood flow

The hemodynamics basically show the relationship between flow and resistance. Under these conditions the BOLD signal change produced by a change in deoxyhemoglobin flow may be approximated by the differential.

6.3.7 DCM and EEG

In contrast to fMRI, with EEG and the usage of biophysically forward models, explicit statements can be made about the underlying neural parameters (David et al, 2006). That means source activity on the scalp surface and EEG data is assumed to be linear and almost instantaneous, which we can capture with this expression:

$$h = g(x, \theta) = L(\theta^L)x_0$$

This only says that the scalp data h, as a function g of the input signals (x, θ) is equal to L (lead-field matrix)[86] (Mosher et al. 1999). Which means further, it takes into account the passive conduction of the electromagnetic field, hereby for laterals θ^L and source signals x_0.
In order to compute the lead-field matrix, individual elements need to be approximated by polynomials, which comes with high computational costs. One way to keep the working power low is to reduce the dimensionality by projecting the data onto a subspace, defined by its principal eigenvectors. The eigenvectors are computing via singular value decomposition (SVD), or PCA, that was discussed earlier.

[86] The lead field is the linear operator relating brain electrical activity to potentials on EEG electrodes.

It should be emphasised that fundamental conditions of EEG experimentation have changed dramatically over the last decade. In accordance to the fast evolvement of capacities of computers highly sophisticated calculations can be performed routinely. Besides the model development has changed. By inclusion of the inversion technique models are specified, which is important, because this influences the believes of how data were generated (Daunizeau & Fristen 2007).

As a starting point some reasonable and fairly realistic model of neural interactions in the cortical regions of interest is initiated. The event-related input is exactly the same for all ERPs, albeit the specific changes in the connections are caused by the effects of experimental factors, which are mediated through event-related response (ERR). By taking EEG measurements of the averaged scalp responses of the neural activity the original model is updated by a forward, backward or lateral model. These differential responses to different stimuli can either be mediated as extrinsic (forward=bottom-up / backward=top-down) or intrinsic changes in connectivity strengths (David et al, 2006). These effects are mathematically expressed by coupling factors:

$$A^F_{ijk} = A^F_{ij} B_{ijk} \qquad A^B_{ijk} = A^B_{ij} B_{ijk} \qquad A^L_{ijk} = A^L_{ij} B_{ijk}$$

Here the diagonal of the matrix gives intrinsic effect of the connections. These three equations only differ in their architectural references *F = forward, B = backward, L = lateral*. *A* represents the strength of a connection from related sources *i, j, k* and *B* modules the multiplicative factor. Since multiplication is used, instead of addition, the resulting effect remains positive, if the connection and factor are both positive. If one factor negative, it represents decrease of the connectivity strength.
Continuing with the model that was mentioned as a starting point basically contains the inputs of afferent activity that are forwarded to the corresponding subcortical structure. In order to do so, the model uses two mathematical constituents: first a gamma density function, through which the spread and delayed inputs are trimmed to the peri-stimulus bursts.[87] Second through a discrete cosine set, that allows to integrate the fluctuations of the inputs as a function of peri-stimulus time.

[87] Peri-Stimulus, more often peristimulus-histogram (PSTH), are a form to visualise the rate and time of highest interest. That means it highlights the rate of firing at the time of firing, in relation to some stimulus or event.

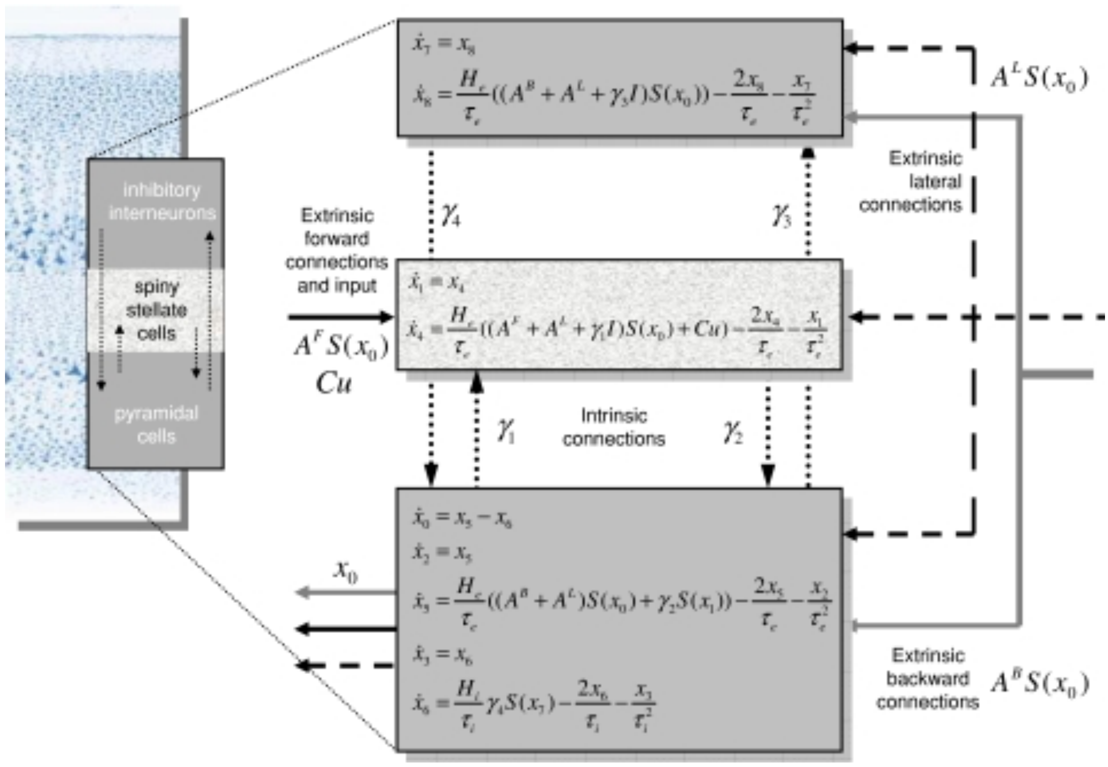

Figure 13: Neuronal state-equation. 3 Subpopulations, 4 intrinsic connections: weights = $\gamma_{1,2,3,4}$. A^F (forward), A^B (backward), A^L (lateral). Output=transmembrane potential

The neuronal activity, represented by the inputs and forwarded connections can e.g. be structured hierarchical as a neural mass model. Here, the dynamics of the excitatory and inhibitory neurons are assigned to a certain number of cortical layers and their connections (e.g. granular, subgranular, pyramidal, etc.). The already mentioned differences of intrinsic and extrinsic connections of ERPs depend on the cortico-cortical model of the neuronal sources. So what DCM facilitates by this structure is in fact an ongoing updating model of effective connectivity.

6.3.8 Limitations

The main idea of DCM for EEG is to model condition-specific responses over channels and peristimulus time with the same model. The very limits of the informative value of DCM lies in the complexity of the underlying model. Indeed, the occurring differences among conditions are explainable by changes of only a few parameters. This makes it useful for single trials, where one would use a parametric modulation of parameters to model the effects of changes between the trials, but also for group studies, where trials as the effects of single subjects are changed by an experimental variable. Accordingly a vast variety of forward models, Bayesian comparisons, as e.g. equivalent current dipoles (ECD) can be applied and compared for a given set of data. Nonetheless, non-Bayesian approaches, where comparisons are only feasible under certain constraints, simultaneously show the advantages and limitations of DCM. Since DCM is deterministic, it is sort of tied to Bayesian inference. This means that the observation noise in the sensors is taken into account, but not at the level of the neuronal dynamics. Noteworthy when DCM is applied to fMRI, because hemodynamic signals still provide low-pass filtered information about neuronal events that are fluctuating (Heinzle et al., 20018). [88] Fitting of complex models to data sets with limited resolution may lead to great fits, while the physiological parameters are out of focus. However combing EEG - used as a first pass by sequential inference procedures with Bayesian inference and then applied to fMRI as second inference step - may help to dam this limitations.

Another issue, or rather limitation is the resting condition. The complexity of doing and thinking about nothing, endures to be mysterious. Someone never knows exactly, or can hardly describe how much, or less of this nothing is dominant in their thoughts. What remains is a vague starting condition and the unclear potential utility of task free states.

Finally DCM is restricted to a few nodes, or regions. Although more simplified versions of DCM (Frässle et al., 2017), achieved computations for hundred of regions, this is not possible while keeping the same indicated and high level of modelled complexity.

6.4 PTE, GC, DCM

Since we have come this far, let's take a look at the three methods and sum up their relationship to each other.

Up to this point the examination of connectivity already proceeded in a rather comparative way and there are some similarities and distinctions that should be addressed before we go any fur-

[88] The Wilson-Cowan model (Wilson & Cowan, 1972) is one approach that allows a compromise of simple and complex neural states that can be helpful to overcome the resolution and complexity limitation.

ther. Prior to listing individual components, the rhythmical compositions of the data and specially the rhythmics of neuronal interactions are to be lit. For it a distinction can be made between the time and the frequency domain on one side and the phase and amplitude relations on the other side. Although this concerns are two separated discussions in the field, context wise we can treat them as being quite similar. Hence this similarity comes to the fore when looking at the time, resp. phase methods that are successful for testing moment-by-moment changes in synchronisation for neuronal interactions (PTE). Moreover these methods can operate with very little information of the envelope (amplitude). At the same time the advantage of doing almost without what is usually most meaningful is not necessarily only an advantage. So the frequency, resp. amplitude driven relations can achieve insights by the application of non-parametric (e.g. Fourier-, Hilbert transformation) and parametric (e-.g. VAR) techniques.
With such connectivity metrics (GC) diffuse resolutions of the data can still lead to revealing findings. Seeking the couplings of dynamical causalities in the brain, DCM uses highly specified and detailed state-space models. By doing so, insights about the underlying physical-causal mechanisms of the brain are sought.

DCM is with its sophisticated complexity one extreme among the whole repertoire of the wide ranged scale of connectivity analysis methods. Even more distinctively it is a model-based approach, which is one of the key differences when comparing the three of them. Right at the other extreme are model-free approaches like PTE. As a far more simple analysis method, it likewise urges far fewer assumptions on data samplings. Solely PTE extracts causality from time series data by detecting the exchange of information between two systems. This makes it immensely sensitive to choices of rates and parameters compared to the likes of GC and DCM.

Rather in the middle of the connectivity arrangement stands GC. Although a generic model serves as the basis of GC when using VAR, and model-based assumptions about underlying connectivity are inherent, it is considered a much more liberal setup compared to DCM. One could perhaps say GC is in itself prediction-based and therewith maximal semi model-based. Inclusion in modelling occurs when it is associated with VAR or the like.

Apart from this allegation, if the data is Gaussian GC can be viewed as an approximation to PTE and becomes indistinguishable beyond a certain point.[89] In addition GC is created to describe data in the form of information flow, instead of physiological dynamics like it is the case for DCM. GC takes into account the dependencies between the measured responses, while DCM models how the neuronal activity in one brain area causes the dynamics in another.
Therefore it can be applied to higher sized networks and directly to any time-series of empirically sampled neuronal systems.

Furthermore GC (approximately PTE) and DCM are part-wise complementary. Despite fundamental differences, multivariate GC can be used for large datasets and DCM optimises network discovery for sparse regressions. Depending on the hypotheses one convenient way to combine both methods is to provide a data driven approach with GC as first analysis and subsequently specifying physical mechanisms using DCM.

7 Discussion and Reflection

Starting with an interpreted summary of the historical development at the interfaces of physics, acoustics and neuroscience, this thesis evolved to review different approaches to characterise acoustic research and methods in connectivity analysis. A number of mathematical approaches were discussed and compared, primarily on the basis of an empirical research project, which should be of interest for follow-up studies.

Brain connectivity, as well as connectivity analysis, is often considered as communicative interaction between different brain regions. We have seen many studies and explored a generous variety of metrical methods and models to expand the patterns of couplings between neuronal populations and associated behaviours. From exploratory analyses of anatomical-, over functional- to effective connectivity various approaches and combinations of increasingly sophisticated modelling of neuronal mechanisms were covered. This also attracted that the shape and exact loca-

[89] Gaussian=normally distributed (Barnett et al., 2009)

tion of brain regions is not exclusively in interaction with itself, but just as strongly with the modelling. Projects like the connectome, or functional connectivity fingerprints are on the verge to demystify the otherwise uncharacteristic activations that illuminate in imaging procedures.

Essentially, some of the discussed measured are not explicitly defined as being based on a mathematical approach. For instance the phase slope, or the phase lag index (PLI) with the imaginary part of coherency are first of all pragmatic. By design these draws put forward the interpretational problem of field spread and interaction between time series. Which of the measures is most appropriate is often an empirical question. Unlike, for example, coherence and GC, which are rooted in the theory of stochastic processes. In general it remains to be advisable to work tentatively with various models, thus the conclusions are not too strongly dependent on the chosen priors.

7.1 Current Methods

One of the keys for understanding which mechanisms underly the drive of information in and in-between brain regions, as populations of neurons and individual neurons is to bridge functions and structures. Focusing on the dynamics of the brain on the one hand and the rather static structural backbone on the other hand, combines segregated parts to one effectively integrated organism.

In order to achieve a deeper understanding of the functional-structural relationship that may lead to an integration of segregated parts each of those, segregation- and integration processes have to get mapped and understood one at a time. So first, how information is segregated to specific parts and then gets integrated across various different regions in the brain. Revelation can occur by utilising individualised concepts of various statistical measures and imaging modalities. Different parts of the brain are considered as functionally connected if there is a measurable fluctuation in their activity, that persists in phase. Thus fluctuations occur synchronously and coherently in temporal resolution. Their structural connectivity is usually derived from diffusion spectrum imaging (DSI), high angular resolution diffusion imaging (HARDI) and diffusion tensor imaging (DTI). The measured strength of structural connections follow as edges, which are converted values representing weights in graphical models. In contrast, functional connectivity uses cross-correlations, partial correlations, coherence in GC, PTE, or DCM, derived from fMRI and M/EEG.

7.2 Gap between connectivity types

Considering the variety of methods and models, the approach of further increasing the complexity and combining them with each other is not without danger. In order to bridge the gap between different types of connectivity methods and more direct biophysical insights, several things need to be considered.

7.2.1 Sample size

According to recent critics of brain imaging (Marek et al, 2022), data sets had been swelling in size. Since one common phrase at the end of a publication says the amount of data needs to be increased to be more conclusive, this should also increase the reliability of the study. But raising the number of participants from a few docent up to a few hundred won't necessarily change the strength of the correlation significantly. Marek and Dosenbach claim that far larger sample sizes, around a few thousands are needed otherwise the notion of correlation is only a weak measure showing that a study is wrong or rather lucky. In contrast, drawing conclusions about brain functions as they are, or even individual brains, derived by sample sizes over a thousands is highly suspect. The correlation between one scan and another won't gauge their reliability. In fact just repeating one and the same scan over time, won't correlate with itself neither (Hariri et al. 2020). Anyhow, one way of dealing with this issue is to prolong the scanning time. Instead of detecting one elucidation for a few minutes, an hour for more similar task testing may turn out to be more robust. There is a danger of habit here, so that further blurring enters into the measurement and a range for the correct measurement must be worked out. Of course the ideal task-scanning-time differs strongly between individuals, therefore additional pre-studies (e.g. biomarkers, HRF, blood pressure, anamnesis, etc.) can be helpful to be able to determine at least a rough fitting inter-subjective range.

7.3 Behavioural integration

Yet there is more to it than sample sizes. The selection process of participants is a careful undertaking. Even more so - as illustrated in this thesis - the choice of model and analysis method. Techniques like DTI that allow tracking of fibres can initiate fundamental changes. Whereby this very technique has been rather limited so far, as it only functioned properly at low resolution, but that is one thing of significance that has changed (Axer et al., 2010).[90] Using 3D-polarised light

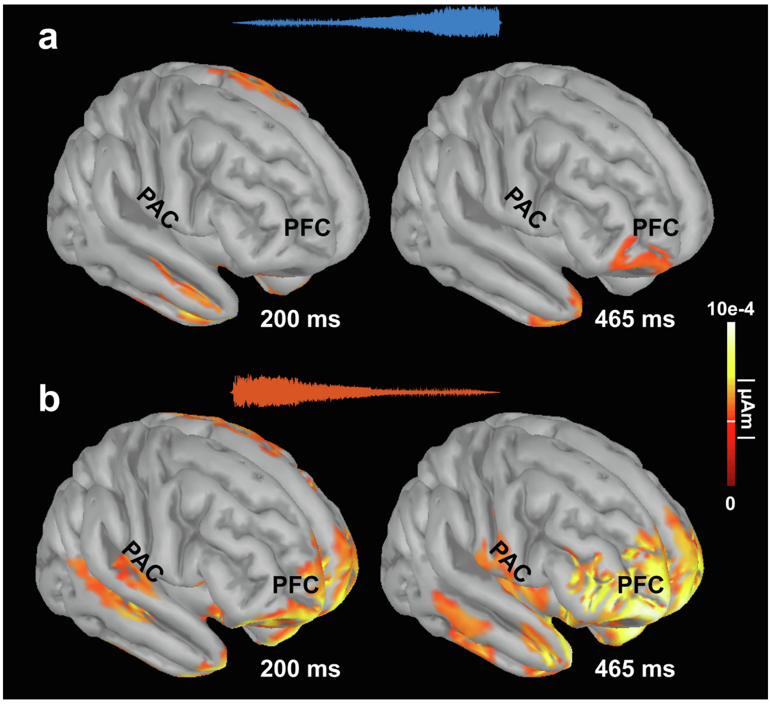

Figure 14: responsive neural interplay of PFC and PAC for judging sonic motion, (a) looming (b) receding. Elucidation for dynamic sounds early at 200 ms and late at 465 ms (Bidelman & Myers, 2020)

imaging (3D-PLI)[91], a spatial resolution in the range of one micrometer is possible and these

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90 M. Axer, K. Amunts, D. Grässel et al., "A novel approach to the human connectome: ultra-high resolution mapping of fibre tracts in the brain," NeuroImage, vol. 54, no. 2, pp. 1091–1101, 2010.

91 3D PLI is a neuroimaging technique that visualises the complex architecture of nerve fibres. Serial brain sections of tissues (taken from postmortem brains) are analysed by optical methods. This happens by casting polarised light on the tissue and analysing the difference in index of refraction (birefringence). The resulting phase shift between orthogonal polarisation states exhibits fibrous structures such as myelinated and unmyelinated axons. Polyfilters are detecting every ever so slight change of the transposed refraction angles. In order to get the depth for the 3D visualisation, another detection run is undertaken with the inclination of the same tissue image. By a voxel based matrix analysis the 3 D PLI is achieved.

methods are constantly evolving and promise a rich future for connectivity analysis from the cortical visualisation perspective.

Until then, it must be stated that the scaling of temporal and spatial ranges as the way they are brought to connectivity remain insufficiently understood. Foremost the concepts of functional-, or effective- and the related structural-, or anatomical connectivity remain to be questionable. The computed quantities of functional imaging types heavily vary in spatial, temporal, frequential and a whole series of other features. Moreover different definitions for variables, constants, measurements and data of the same modality is employed with different computational algorithms. This connects directly to the debate on causality which was suggested by Granger at the time. Much of science still depends on its notion, what it represents, how it is defined and what it implies. As in this investigation, the walkthrough from the acoustic evolution in physics to its follow up adaptation to neuroscience and mathematical modelling, the puzzling challenge of taming the Leviathan in the data is still up to his tricks. Despite the dichotomous definitions, the fundamental interest in all connectivity research persists as *"… understanding the causal relationship among neural entities."* (Reid et al., 2019). With Friston that is indeed nothing but a fixing exercise. So change in this sense is not just about the development of the research field, but the need to establish a more compact and neat concept of this procedure. Some new type of modality that is not based on a post-phrenological versus sophisticated and all-function conceptual framework that produces non-reproducible data. Connectivity as a measure of brain functions alone, might be expanded to include extra-cortical areas and bend to the limits of its limitations.

The models of functional, resp. effective connectivity are mathematically still exclusively investigating in the brain. Other aspects of the organised individual and its surrounded environment are usually not taken into equational account. The trinity of body-brain-behaviour, within an environment may lead to more conclusive findings and reliable parameters, as the brain alone is able to reveal. So the connectivity analyses methods of the brain structure could be expended to behavioural traits and cognitive parameters that are integrated in the metrics. In addition, the model fixing exercise can be accompanied by a cognitive model approach.

7.4 Cognitive model

As a consequence it is about the mind, whatever that turns out to be, which brings the fire into the neuroscientific equations. In a similar way like Marek points out, saying that not only higher sample sizes, but behavioural trait offs are like adding an environmental- to the biological marker to stabilises connectivity measures and the likes of cognitive parameters as representers of the mind could have a similar effect. The biophysical evolution from anatomical to functional and lastly up to effective connectivity measures on the one hand and model transformations like improvements from speculative projections to constantly updating error rate functions, Bayesian inference and predictive coding on the other hand, are still operating in a self-limited area, mathematically, biophysically and conceptually. The trend of expanding the complexity of the models, the resolution of the imaging methods and precision of the measurements led to an important and viable step-by-step development of the field which stands for itself. But what hopefully did not remain hidden in the course of this work is the sever limitation of the conceptual frameworks and to what kind of physicalities the mathematics are factually referring to. Therefore with the following I like to question some paradigms that are used in neuroscience, but which are in transition and could be extended or even modernised in one or the other way.

7.4.1 Overriding

At this point it may be exciting to question the used notions of SC, FC and EC. At several publications (see the references) appears the instructors description for connectivity analysis methods as separated in three. This master's thesis also uses this term out of convention, but not without criticism. As neuroscience has changed dramatically over the last decade, classical ideas about the theoretical framework behind experimentation and the current state of science can get out of joint. These representations in particular must therefore always be adapted to the current state of research.

The empirical study of this thesis, as from others (e.g. Bidelman & Meyers, 2020), reassert that functional connectivity of neuroelectrical brain activity during looming and receding of sounds reveal stark differences (see fig. 13). Approaching sounds are more rapidly evaluated (< 200ms), than those in retreating motion. This counts for the prefrontal cortex (PFC), rather than the primary auditory cortex (PAC), which might have been expected sooner in the case of sound perception. This is explained as override from higher-order brain regions (PFC) of auditory cortical processing at initial stages (Winkowski et al., 2018). Moreover the assumption is strengthened by the direction of the information flow. During looming PFC -> PAC preferential operates in a top-down manner, whereby bottom-up (PAC -> PFC) showed no differences to directional changes of the auditory motion. That means overriding is an indication of top-down, resp. PFC activity.

Furthermore, and if that is the case, a transformed definition for basic concepts of connectivity methods could support further steps in research. With the following section I like to discuss if that is the case for the long prevailed trinity of connectivity approaches at first place. Overriding, as a feature of the brain might go one step further than the effectiveness of connectivity. Several conclusions could now be drawn from this assertion. An obvious approach would be to ask what else happens before the PFC activity <200 ms, what is the precondition, what means resting-, or initial state and what is it, that is actually being measured? Asking about this involves further questions, such as those about technological possibilities, mathematical integration and, last but not least, the concept of brain and connectivity in more detail.

7.4.2 Extended neuroscience

Primarily various novel technologies are transforming the methodological possibilities. As the mentioned 3D-PLI, optogenetics, implantations, or interfaces. In combination with the integration of the parameters of interest in the equations, mathematics has to adept to these technologies, more than the other way around. But latter adaptation only makes sense if the concept of the brain, as the understanding-, or level of connectivity and neuroscience generally develops in complementarity. This is obviously going on right now and has been for the past few decades. Anyhow not necessarily in lockstep. Sometimes one area lags behind or another jumps far ahead, leading to disparities that slowly converge again until they diverge again, as it oscillates on.

Conceptually, neuroscience as a whole is changing. The view of the brain as the central control unit is no longer dominant, although leading imaging techniques do not yet take into account advanced neuro- or cognitive theories to the same extent. Therefore, it could be assumed that the technology does not go hand in hand with the present concepts, while the mathematical approaches are all too versatile. Approaches like those that do neuroscience without neurons (Prakash et al., 2021), involve the body and environment as dynamical system (e.g. Beer, 2008), but also exploring ideas like augmented or extended cognition (e.g. Clark & Chalmers, 1998).

This can be understood as a state of mind from which certain conditions for a measurement entail. The focus is not primarily on clear, directly measurable parameters of one's own biomarkers, but on far-reaching interrelationships of effects that lie in and outside a classical neurocentristic perspective.
Consequently the very thing that is to be measured and subsequently interpreted can partially already be part of the preconditions, the equations and the measurement itself. The uncertainty, but nevertheless the complementarity in this form, can give a more comprehensive picture.
Hence this is different from doing cognitive neuroscience branch-wise, wherein cognitive tasks and brain activity - as environmental features - are wired together in a perceptual manner, but the measured entities themselves are immanent to each other. To understand the nervous system, living beings and somehow organised structures that form something like life or even consciousness must include representatives such as mental states in the connectivity.
Even more so and given the assumption that this could be feasible, the mathematical concepts that are used in neuroscience are of such a wide variety that - as shown in the discussion of some approaches in this study - measurements can vary to great extend, or even contradict depending on the model chosen. From a mathematical point of view computational neuroscience may not have been the last encapsulation, as there could also be the separate research area of mathematical neuroscience (Silva, 2011). Even more on a conceptual, less on a biophysical level, venturesome steps such as the integration of quantum formalism in neuroscience tend in such a direction (Busemeyer, 2013). The development of structural to statistical to causal coritcal connections could lead to the introduction of modern concepts in imaging with non-standard probabilistic graph theory.

7.4.3 Cognitive parametrisation

For instance, most M/EEG laboratories have adopted a dual strategy. Resolved this means the first measurement step is based on most robust and conventionally safe methods, whereas the second weights the ideal mixture of exploration and exploitation (Picton et al. 2000). Afterwards the same robustness is sought in the analytical process. Nowadays, e.g. fMRI analysis groups agree on main methodological exploitation, that obviously gives little room for exploration (Police et al. 2006). Another strategy could open up the research space by defining cognitive parameters through current and future models of the mind implemented directly into a mathematical structure. More prominent and in many ways synonym to mind-models are theories of consciousness like higher-order-theory (HOT) (Rosenthal, 2005), integrated information theory (IIT) (Tononi, 2012), predictive processing (PP) (Seth, 2020), or global workspace theory (GWT) (Dehaene, 2011), just to mention a few contenders for mind integrated connectivity measures (lets call them MIC). Of course future progress when employing theories in this manner will strongly depend on the validation of the mind-part. Currently there remains to be a measurement issue that makes it difficult to identify trustworthy equations, parameters and resulting measurements of consciousness (Browning & Veit, 2020).

However, it can be argued that this problem is rather caused by controversy. Primarily there must exist some kind of taxonomic clarification, that distinguishes conscious from unconscious, or non-conscious. There could be distinctive notions about; what it takes for human consciousness to emerge for the first and last time in a lifetime; how it and certain properties of it, as for traumatic injuries, psychedelic influences etc., develops; how other animals and artificial beings can be consciousness.

At the realm of conceptual and computational modelling is going to be the first important hurdle after the updated version of connectivity measurement is on the run. Depending on the theory as there are re-entry models (HOT, PP) which need to indicate specific parameters and meta-paramters for the update functions that are in concrete relation to some state of mind, or for more environmental orientated theories (IIT, GWT) the impact factors, as the relevant senses must be clearly defined. Whether the mind is seen as a functional neuroanatomical region somewhere “at the brain“ (front of the brain vs. back of the brain theories, Sergents, 2021), or a process that is extended and also accounts for phenomenological features.

7.4.4 Novel connectivity

The pressing question in terms of connectivity analysis is what kind of connectivity follows next and in view of the previous explanation how might it involve an expanded form of neuroscientific investigation? Given the lack of coherent concepts, unambiguous mathematics and a multitude of models that are more or less reproducible and meaningful, as well as evolving technology that is constantly expanding measurement possibilities, a kind of connectivity that goes beyond the effectiveness of a causal concept could be a possible successor. At this point in development of various models and concepts in parallel, assuming that there are some of them, which are partially correct in a sense that their results lead to deeper understanding of the content and further steps in science, more than one consequences are possible.

So folded in three: first there is a desirable and productive outcome which leads to models in unexpected, but experimental testable and verifiable, reproductive and computationally predicable results. Second, the novelty of the model is rather modest and only partially corresponds the experiments, or is only to some extent testable at all. Third, less desirable, the model is untestable, computationally limited and without counterparts in the real world. All three possibilities share the model construction and perhaps the simulation of these models at first stage. Since this remains to be purely descriptive, in the literature often referred to as "numerical simulations of postulated models" and the amount of data are getting larger some qualitative prescriptions would be something else.
In other words the starting conditions in neuroscience could be formally more concise. Given a theoretically well constructed and scientifically agreed framework - as described above - this could be translated into mathematical expressions. The theoretical and mathematical expressions can be used as axioms which must be proven. Further implications and numerical simulations can be built on the proof, as it is possible to work back to the foundation of the axioms.
This, or something near to it can be achieved by applying these different frameworks in order to detect parallels, congruences or their anti-parts in a connectivity way. As it was the case in physics, chemistry and others, it is in neuroscience that specific-, or even personal concepts and mathematics are needed to express the ideas, concepts and findings of this very field of study. Currently the mathematics of neuroscience are still very much limited to approaches from other areas, as the concepts and the underlying understanding of how the brain, mind, etc. functions. The great challenge, and the great gain, would be to develop, or adapt, a unique mathematics and concepts that come much closer to describing what neuroscience can be than synthesising other

disciplines into a model-fitting exercise. Connectivity wise this can be investigated by expanding the regions of interest by a combined strategy of fundamental complementary notions of mathematics and analytical reasoning, as a post Von-Neumann architecture, with non-classical, e.g. chaotic processing in neuroscience, which allows neuroscience to go further than todays imaging methods.

8 Conclusion

In a final summary, this thesis introduced with a short recapitulation of the development of acoustical research (sec. 1.1). As it turned out this also included physics, physiology, neuroscience, mathematics, computational and cognitive science. So it ended up being an exploration of the interdisciplinarity of this endeavour. Part two of the chapter (section 1.2) outlines the structure and aims of the thesis in a formal preview.
The second chapter explained the fundamental components of further investigations. From the basic but all too important question of *What is sound?* (sec. 2.1), through the curious phenomena of hearing (sec. 2.2) to the neuroscience-oriented backgrounds (sec. 2.2).

With the models of auditory-cognitive processing (Chapter 3), I have invested part of the thesis in the important field of modelling in neuroscience (sec 3.1) and modelling as one of the most central aspects of today's research in general (sec 3.2 & 3.3). The chapter was rounded off by the more directly applied and thoroughly relevant models for this work: e.g. ALB, ITD, ILD (sec 3.4).

An examination of the empirical part of the thesis follows in chapter 4. This leads through the whole course of the experiment in a classical, resp. conventional arrangement: Introduction, Materials, Results, Discussion.As some research has already been done in this area, but the experiments as well as the whole study are still ongoing, more emphasis has been put on the content and understanding of the techniques and activities as a whole, rather than focusing exclusively on a publication or a small completed part of the study.

Chapter 5 - Brain Connectivity Analysis - finally opened up the core area. Most relevant parts of the architecture (sec 5.1), networks and graphs (sec. 5.2) and the method of measuring connectivity (sec 5.3) are described.

The core area was further investigated into deeper and deeper layers. The measurements turned into metrics (sec 6.1) and the interdisciplinary prepared neuro-dynamical backgrounds of modelling in time, space and frequency (sec 6.2) transformed more and more into concrete connectivity models (sec. 6.2 - 6.5). The whole structure of the metric modelled area resulted in a comparison of the most important analysis methods (sec. 6.6).

Arrived at the discussion and reflection part the current approach (sec 7.1), like the gap between these approaches (sec 7.2) in connectivity, but neuroscience oriented disciplines in general, initiated a more critical exchange with modern coverings in the field, but also there omissions. The last sections (7.3 - 7.4) elaborate possibilities of what is currently failing, what the study fields could need and solution wise how this could be feasibly modelled to set incentives and impulses for further development steps.

Finally there is chapter 8 in which we are in right now. Concerning the long term schedule of the underlying neuro-acoustic project (at least until 2024), there is still loads of work to be done. Then again, a lot of work has already been done.

The scientific evolution to a point where vast amounts of data are collected, variously interpreted and virtually tested is astonishing and holds great potential. So, of course, this potential is not only used in basic research, but also applied in all sorts of areas where it has a direct impact on the lives of humans, other animals and the planet in general. …

We are analogue beings trapped in a digital world, and the worst part is, we did it to ourselves. Is the brain digital and the mind analogue, or vice versa? At least it seems that we perceive things discretely, although there is reason to believe that they are not quite as discrete, since we are able to transform them into our perceptual reconstruction. The world is not what it looks like, what it sounds like, what it seems like, but rather the self-taught illusions we constantly derive from it. In order not to get ahead of oneself, but rather around the illusory parts, scientific practices and modelling in particular open up opportunities, indeed bear the very responsibility of recognising and adopting them. The scientific point of the whole endeavour shows that the thesis itself is nothing more than a model. A model about and around models, as an iterative development process that straddles the line between reality and simulation. Some of the challenging proponents in modern science are addressed and put into specialised context. Efforts to experiment, test and comparison will lead to a much more profound comprehension of these deepest mysteries.

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