DISS. ETH NO.

VESTIBULAR IMPLANTS LINE 1
VESTIBULAR IMPLANTS LINE 2

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presented by
THUY ANH KHOA NGUYEN
Diplom-Ingenieur Mechatronik (TU Dresden)
born 18 August 1985
citizen of Germany

accepted on the recommendation of
Prof. Dr. Manfred Morari, examiner
Prof. Dr. Silvestro Micera, co-examiner
Dr. Barry Seemungal, co-examiner

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ABSTRACT

Yahoo a very sexy abstract will emerge here

ZUSAMMENFASSUNG

Eine schöne Zusammenfassung für die Leser.

PUBLICATIONS

The following publications are included in parts or in an extended version in this thesis:

- To come

Furthermore, the following publications were part of my PhD research, are however not covered in this thesis. The topics of these publications are outside of the scope of the material covered here:

- To come, too

ACKNOWLEDGMENTS

I am so grateful for the people around me. They are amazing. Really.

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INTRODUCTION

> The senses do not err — not because they always judge rightly, but because they do not judge at all.
>
> *Critique of Pure Reason*, Immanuel Kant

Our senses accompany our everyday life: We hear an alarm ringing, we slowly open our eyes and touch our smartphone to turn the alarm off. The scent of fresh coffee helps us to rise out of bed, have breakfast and enjoy the wonderful taste of a pain au chocolat.

This scene exemplifies the five senses that Aristotle (384 BC - 322 BC) is believed to have originally classified. The notion of a sixth sense consisting of the vestibular and other proprioceptive systems emerged only after the mid-19th century when scientists realized that vestibular organs in the inner ear were not related to hearing, but involved in equilibrium functions. Today, we are more aware of the vestibular system's instrumental role in our everyday life.

A disruption of vestibular inputs can deteriorate motor coordination, postural control and spatial orientation. While individuals with unilateral vestibular deficiency or mild and moderate bilateral vestibular deficiency can at least partially compensate, patients with bilateral vestibular loss (BVL) have currently no viable treatment option. They can experience chronic dizziness, vertigo, imbalance or oscillopsia (blurred vision), thus significantly reducing their quality of life (TODO cite Sun et al 2014, Guinand et al 2012).

TOWARDS VESTIBULAR IMPLANTS

BVL patients may benefit from a vestibular implant (VI). Conceptually these are similar to cochlear implants that restore auditory function and have been the most successful neuroprosthesis to date with more than 300'000 people implanted worldwide (cite NIH report 2013). In a VI, electrodes or electrode arrays placed in the peripheral vestibular nerve branches, employing electrical stimulation to convey information about head movement to restore vestibular functionality (todo figure).

First experiments of electrical vestibular stimulation in 1960s. Suzuki, Cohen et al. activated vestibular structures with an implanted wire electrodes in cats (todo cite). They used monophasic constant voltage pulses, damage tissue (Shepherd 86 and '99) In 2000 first self-contained VI in guinea pig, one canal (Gong and Merfeld 2000, 2002). Extended to three canals (Della Santina 2007). A third group (Rubinstein). feasibility in humans Guyot et al 2009; Assessment, evaluation with Responses mediated through vestibular ocular reflex (VOR)

In 2009, CLONS started, ambitious, challenging, endeavor. Main objectives: tests in patients, animal models, assessment devices, modeling, most ambitious goal closed-loop. Number of partners involved. Regarding closed loop, concept briefly, vestibular signal or feedback signal to have cascaded closed-loop, identification and characterization of feedback signal. VECAP, vestibular electrically evoked compound action potential; investigation of correlation between VECAP and physiological signals in GPs.

In meantime human patients instrumented with modified cochlear implants, for instance in Geneva or Maastricht. Since patients both deaf and BVL, these were hybrid cochlear-vestibular implants with nine for cochlear and three independent electrode sites designated for vestibular stimulation. With approval to use modified cochlear implants, question arise which stimulation paradigm more effective: pulse amplitude (PAM) or pulse rate modulation (PRM). Goldberg and Fernandez' seminal studies found that primary afferents encode information with spike rate modulation (cite Goldberg and Fernandez). This predominantly emulated with PRM in implant prototypes in animal models. However, cochlear implants (orginally also employing PRM) commonly use PAM.

ORGANIZATION OF THIS THESIS

This short intro motivated research, described author's contribution to the field.

For the keen reader, Chap. 2 provides an overview of VI research since it has taken off in the 2000s.

Part i details how to reduce artifact and measure vecap (Chap. **??**, and presents correlation to VOR responses (Chap. **??**.

Part **??** presents the acute stimulation trials to investigate PAM and PRM in human patients. To this end, a customized real-time platform was programmed (Chap. **??**), experimental results are discussed in Chap. **??**. TODO a figure to unify the two chapters here or later in part iii, better part iii

Finally, Part **??** provides a summary as well as an outlook in the research field of vestibular implants.

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BACKGROUND

This section provides an overview of VI research in animal models as well as human patients. A handful of research groups have excelled demonstrated expertise, most prominent merfeld and lewis, della santina, rubinstein and philipps, guyot, perez-fornos, kingma. Comprehensive reviews have been published recently (Merfeld and Lewis, van de Berg, Fridman and Della Santina). A table in appendix gives overview of research, similar to table in van de Berg. More general vestibular neurophysiology are excellently detailed in The Vestibular System and Clinical Neurophysiology of the Vestibular System.

Introduce general concept here. Motion sensor senses head movement, processor/ controller computes stimulation strategy and parameters. Sends parameters to nerve stimulator to vestibular nerve. This thesis will focus on devices that aim to restore SCC function. This has been the main avenue of research, because each SCC encodes a distinct axis. In contrast, utricle and sacule encode different directions and the remainder of this thesis will TODO figure

General device description for most protoypes in animal models

Motion sensor First devices employed single axis MEMS gyroscopes (Gong and Merfeld). What is MEMS, basic concept how it works. Combining three of them

Gong and Merfeld 2000 proved feasibility of single canal VI. A GP was instrumented with a platinum wire in which? canal. Acute electrical stimulation with these characteristics evoked eye movement responses through the VOR. Magnitude of responses were large. Expansion to study VOR adaptation to baseline (Saginaw), squirrel and rhesus monkeys, chronic stimulation (Merfeld 2005, 2007). Also tested a bilateral implant (Gong 2008). What is their expertise? Diverse animal models, chronic and VOR assessment as well as some balance function (Thompson).

Laboratory of Vestibular Neurophysiology at JHU first to demonstrate a multichannel/multicanal VI or MVP. Animal model chinchilla, rendered BVL through intratympanic injection of ototoxic aminoglycoside gentamicin Detailed description of their first generation device in Dai, second generation here MVP2 Chiang 2011. Misalignment improvements (Fridman 2010), effects of pulse parameters. modulation paradigms (davidovics, another paper as

well). continuous stimulation in chinchillas and recently in monkeys. Valentin et al papers on modified CIs for vestibular stimulation. Strength is 3D stimulation paradigm.

Group in Washington. A third group at University of Washington under the aegis of Rubinstein and Philipps have instrumented rhesus monkeys and also human patients with vestibular implant prototypes. Rubinstein 2010, 2011 (prosthetic implantation of semicircular canals). VECAP, Nie et al 2011, for intraoperative monitoring for placement, because VECAP not affected by anesthesia such as VOR Philipps 2011, Golub 2013 (human). longitudinal study and three electrodes per canal in patients.●

Part I

VECAP – VESTIBULAR ELECTRICALLY EVOKED COMPOUND ACTION POTENTIAL

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ARTIFACT REDUCTION FOR MEASURING VECAP