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ADAPTING TO PROGRESSIVE PARALYSIS

A TONGUE-BRAIN HYBRID ROBOT INTERFACE FOR INDIVIDUALS WITH AMYOTROPHIC LATERAL SCLEROSIS

BY
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Adapting to progressive paralysis:
A tongue-brain hybrid robot interface for individuals with amyotrophic lateral sclerosis

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Rasmus Leck Kæseler

Rasmus received his BSc in "Machines and Productions" at Aalborg University, Denmark, in 2016. In his bachelor thesis, he developed a novel adaptive and underactuated end-effector for robot arms. He received his MSc in "Electro-Mechanical System Design" in 2018 at Aalborg University. In his master's thesis, he developed and evaluated a new mathematical method for automatic calibration of ultrasonic oil-thickness measurements.

He started his PhD at Aalborg University in October 2018 where he developed a tongue-brain hybrid control interface of a robotic arm for individuals with ALS. He has since 2021 been employed as a research assistant at Aalborg University, where he has taught courses and supervised students on the topics of applied mathematics, human-robot interaction, and kinematics. He has since 2021 also worked for the Center for Rehabilitation Robotics where he is developing new exoskeletons and control methods, arranging collaborations with individuals living with ALS or a spinal cord injury, and co-supervising new PhD students.

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Abstract

Amyotrophic Lateral Sclerosis (ALS) is a motor neuron disease that causes progressive paralysis of all motor functions. Individuals with ALS will therefore have an increasing need for assistive robot technologies to maintain independence, but will also have increasing difficulties in controlling such a robot. When it is no longer possible to fully utilize one control modality (e.g. tongue movements), it is necessary to completely replace this with another potentially worse-performing control modality (e.g. brain signals) which leads to critical performance reductions and decreased independence.

This PhD study investigated a novel adaptive control framework, that can utilize residual control modalities in combination with other modalities to maintain high performances as long as possible. The focus was on combining tongue movements with brain signals to manually control a 7-degrees-of-freedom robot arm. A framework was developed consisting of several subsystems that use increasingly more brain control to reduce the need for precise tongue control. Thus, an individual with ALS can use any remaining tongue functionality in combination with brain signals to maintain a high control performance.

The first two studies made during this PhD showed that individuals with ALS can gain control of a robot arm using tongue movements, brain signals, or a hybrid combination of these. It showed the advantages of combining the two control modalities as it can optimize the control performance relative to remaining tongue functionality. User evaluations with an updated framework indicated that usability was also improved by combining the two modalities as all users with ALS chose a hybrid subsystem as their favourite.

A slow phasing in of the new control modality will give the user a better possibility of adjusting and learning the new control method, but will also give the system a better possibility of adapting to the user and preparing for further loss of motor functionality. The last study evaluated the possibility of a more covert and direct transition from tongue control to brain control, by using brain signals to classify the intention of tongue movements. The study showed great potential in classifying complex tongue movements and the possibility of utilizing the intention of tongue movement in future versions of the framework.

Resumé

Amyotrophic Lateral Sclerosis (ALS) er en motor neuron sygdom der resultere i progressiv paralysering af alle motoriske funktioner. Personer med ALS vil derfor have et forøgende behov for assisterende robot teknologier til at fastholde uafhængighed, men vil også have stigende problemer med at styre sådanne robotter. Når det ikke længere er muligt at udnytte en kontrol modalitet (f.eks. tunge bevægelser) er det nødvendigt at erstatte den med en ny potentiel dårligere kontrol modalitet (f.eks. hjerne signaler), hvilket vil føre til kritiske fald i ydeevne og mindre uafhængighed.

Dette PhD studie undersøger et nyt adaptiv kontrol system der kan udnytte resterende kontrol modaliteter i kombination med andre modaliteter for at fastholde en høj præstation så længe som muligt. Der var sat fokus på kombinationen af tunge bevægelser med hjerne signaler til styring af en robot arm med syv frihedsgrader. Der blev udviklet et kontrol system bestående af undersystemer der brugte en stigende mængde hjerne styring for at reducere behovet for præcis tunge kontrol. Et person med ALS kan således bruge resterende tunge funktionalitet i kombination med hjernesignaler for at fastholde en høj ydeevne med kontrol systemet.

De første to studierne lavet under denne PhD viste at personer med ALS kan få kontrol over en robot arm ved brugen af tunge bevægelser, hjerne signaler og ved brug af en hybrid kombination af disse. De viste fordelende ved at kombinere de to kontrol modaliteter, da det kan optimere kontrol systemets ydeevne i relation til tilbageværende tunge funktionalitet. Bruger evalueringer med et opdateret system indikerede at anvendeligheden af systemet også blev forbedret med kombinationen af de to kontrol modaliteter da alle brugere med ALS valgte et hybridt subsystem som deres favorit.

En langsom indfasning af den nye kontrol modalitet vil give brugeren bedre mulighed for bedre at vænne sig til og lære den nye styrings metode, men det vil også give systemet mulighed for at tilpasse sig brugeren og forberede for yderligere tab af muskel funktionalitet. Det sidste studie evaluerede muligheden for en mere direkte overgang fra tunge bevægelser til hjerne styring ved at detektere og klassificere intentionen af tunge bevægelser ved hjælp af hjerne signaler. Studiet viste et stort potentiale for klassificering af komplekse tunge bevægelser og muligheden for at udnytte intentionen af tunge bevægelser i fremtidige versioner af systemet.

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I feel very privileged to have worked on this PhD thesis and would like to express my deepest gratitude to the many people who have helped me accomplish this life goal.

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My family and friends have also been subject to my research and work-related discourse over the years: thank you for lending me your ear. Here I would like to especially thank my parents. To my mother, who has always encouraged me to follow my dreams (which includes applying for this PhD study, though I thought it near impossible at the time), and to my father, who has always been the perfect role model and offered assistance whenever it was needed. Thank you both for always believing in me and for your constant support.

My greatest gratitude goes to the participants of my experiments. I sincerely value our time and talks together. Without your selfless volunteering, this work would certainly not have been possible and I can not thank you enough.

Contents

Chapter 1. Introduction

Tetraplegia, i.e. paralysis of all four limbs, can be caused by either an injury (a traumatic spinal cord injury (SCI)), a disease that causes damage to the nervous system (such as nontraumatic SCI, stroke, or amyotrophic lateral sclerosis (ALS)), or loss of muscle mass (i.e. muscular dystrophy) [1–4]. Activities of daily living (ADL), such as transportation, drinking, eating, or scratching an itchy nose are just some examples where the individual with tetraplegia is required to ask personal caregivers for help. Individuals in a locked-in state (LIS), where eye movements are the only remaining motor function, or complete LIS (CLIS) where eye movements are also lost, may not even have functional communication to ask for help [5].

Diseases such as ALS will cause progressive paralysis where early symptoms (such as muscle spasm or numbness) progressively worsen into full paralysis and eventually death [3]. This loss of independence has been reported to correlate with hopelessness [6]. Similarly, other studies have reported a negative impact on the quality of life (QoL) and psychological well-being for both the individual with tetraplegia and their next of kin [7–9].

1.1 The progression of ALS

Around 1-2 in every 100,000 people are diagnosed with ALS every year, typically at the age of 50-65 years old and with around 5-10% of the cases being familial ALS, while the remaining form is sporadic [3,10]. It is a fatal disease with a life expectancy of 3-5 years but with around 20% surviving between 5-10 years. 75% of ALS patients are diagnosed with Limb-onset, 25% are Bulbar-onset, and 5% are respiratory or trunk involvement [3].

After the diagnosis, the individual with ALS may continue a usual lifestyle for a time; however, their condition will only worsen which can impact their QoL and mental well-being. Vázquez Medrano et al. showed that over a one-year progression of ALS, patients with a fast disease progression had a significant increase in depression and decreased QoL correlating with their physical disability, while patients with a slow progression did not [11]. Other studies have shown that QoL may decrease with the progression [6, 9, 12]. Similarly, the constant dependency on caregivers has been shown to cause helplessness, depression, anxiety, and a lower QoL for both the individual with tetraplegia, but also the next of kin [7, 13, 14].

For these reasons, assistive robotic devices have been developed and used to increase the independence of individuals with tetraplegia and reduce the burden of caregivers [15–19].

1.2 Assistive Robotic Manipulator

Individuals with tetraplegia require assistance for ADL which can be provided by a personal caregiver; however, there are both financial, physical, and psychological advances for also introducing assistive robots, such as an assistive robotic manipulator (ARM), to bring independence to the individual with disabilities and reduce the workload of the caregiver [18–22]. Several commercially available ARMs that are approved as medical devices exist today, such as the iARM (Exact Dynamics, Didam, The Netherlands; exactdynamics.nl) and the JACO (Kinova Robotics, Boisbriand, Canada; kinovarobotics.com), designed to provide a general purpose tool that can assist individuals with disabilities in different aspects of ADL [18].

Both the iARM and JACO have six or more actuated joints that allow the user to control the position and orientation of the end-effector (gripper) and the possibility of opening and closing the gripper. In the following this combined 6 DoF Cartesian control and 1DoF functionality control of a gripper will be called 7DoF ARM control. However, very few human-machine interfaces (HMI) suited for individuals with tetraplegia are designed to provide direct time-continuous control of all DoFs and end-effector; henceforward referred to as *full control of an ARM*.

Out of the box Kinova Jaco2 is provided this control using a joystick consisting of a 3-axis joystick combined with a series of buttons for mode-switching (i.e. selecting which functions the joystick should control) [21]. However, in late-stage ALS, where the users no longer have the necessary fine finger and hand motor functionality to utilize this HMI, the whole system becomes obsolete, unless an alternative HMI can be implemented that only uses motor functionalities still available (typically facial muscles or brain signals). Nevertheless, these HMIs will likely have worse performance.

To improve control performance, several studies utilize automation. However, users with disabilities may value agency over performance [23]. Therefore, automation should not be a necessity for the control, but rather as an optional extra that the user can tailor to their needs and wishes. Similarly, several HMI studies for ARM control refrain from utilizing the full functionality of the ARM (i.e. providing only movement in one plane, without orientational control of the end-effector, or without functional control of the end-effector).

The following review of existing HMIs will include several such papers but is made to evaluate the possibility of allowing full control of an ARM without automation. It will not include HMIs that uses muscle functionality below the neck, including head movements, as the goal is HMIs for individuals with late-stage ALS.

1.3 Existing Human-Machine Interfaces for control of an Assistive Robotic Manipulator

While the existing assistive technologies have the potential to improve the lives of individuals with ALS (or tetraplegia in general), there is still a need for research before they can be utilized in our daily lives [24–26].

When developing an HMI it is essential to evaluate the remaining motor control of the user group. Furthermore, when developing an HMI for individuals with ALS the progression of lost mobility should also be considered. Figure 1.1 illustrate how an individual with ALS may transition between interfaces as the disease progresses from onset to late stage.

Four modalities are of special interest within state-of-the-art control of an ARM using single modality control input for individuals who have lost all muscle functionality below the neck: Lip/jaw movements, tongue movement, eye movement, and brain signals. Lip/jaw-, tongue-, or eye movements have been used to provide efficient control of robots, while brain signals require little to no dependency on muscle movements. Table 1.1 provides an overview of relevant studies using a single-modality to control a robot. Table 1.2 provides an overview of relevant studies using multiple modalities to control a robot.

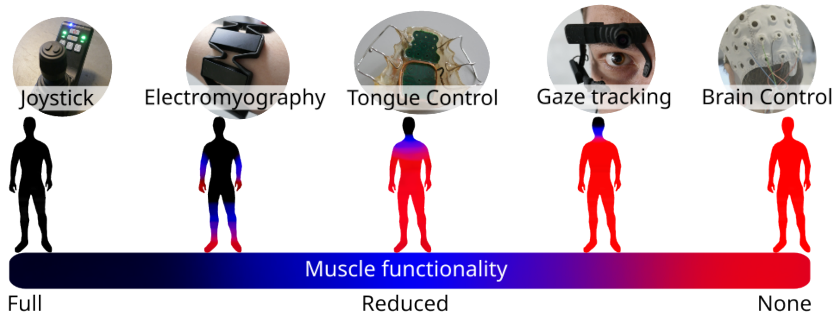

Fig. 1.1: An illustration of how individuals with ALS may change control modalities as their disease progresses from early-stage to late-stage ALS.

Lip/Jaw movement-based interface

José and de Deus Lopes designed a wearable headset with a 2-axis joystick that could be used using lip movements to control a wheelchair [88]. There also exist several commercial products that utilize lip movements in combination with sip-and-puff systems (i.e. including a 1-axis pointer that is activated by sipping or puffing air through a tube) [89–91]. Despite the commercial

Table 1.1: Interfaces used for robot control. The existing literature on robot interfaces using modalities available to individuals with tetraplegia. ✗ : uses modality, ✓: meets requirement, ÷: does not meet requirement, ?: not reported.

	Modality					Usability				Control				Robot	Evaluation		
Reference	Lip/Jaw	Tongue	Eye	Evoked Brain	Spontaneous Brain	Modality adaptable	Eyes free operation	$\leq$ 20min calibration	$\leq$ 5 training sessions	Manual	Continuous	Asynchronous	$\geq$ 7 DoF control	Description	ALS	Other	Healthy
[27–32]		✗				÷	✓	✓	✓	✓	✓	✓	✓	$\leq$9DoF control (7DoF ARM and/or 2DoF wheelchair, or 5DoF upper limb exoskeleton)	0	1	12
[33]		✗				÷	✓	✓	✓	✓	✓	✓	÷	5DoF control (5DoF ARM)	0	0	1
[34–37]		✗				÷	✓	✓	✓	✓	✓	✓	÷	$\leq$2DoF control (2DoF wheelchair or 1-2DoF upper limb exoskeleton)	0	11	10
[38]			✗			÷	÷	✓	✓	✓	✓	✓	✓	9DoF control (7DoF ARM + 2DoF wheelchair)	0	0	10
[39]			✗			÷	÷	✓	✓	÷	✓	?	÷	Object selection with 7DoF ARM	0	0	1
[40]			✗			÷	÷	✓	✓	✓	✓	✓	÷	3DoF control (6DoF ARM)	0	0	8
[41]			✗			÷	÷	✓	✓	✓	✓	✓	÷	5DoF control (5DoF ARM)	0	0	30
[42–45]				✗		÷	÷	✓	✓	✓	÷	✓	÷	$\leq$6DoF control (wheelchair, humanoid robot, or 5DoF ARM+2DoF telerobot)	4	0	4-20
[46, 47]				✗		÷	÷	✓	✓	✓	÷	÷	÷	$\leq$7DoF control (7DoF ARM, 2DoF protheses)	0	0	6-12
[48]				✗		÷	÷	÷	✓	÷	÷	✓	÷	Activation of wheelchair	0	5	8
[49, 50]				✗		÷	÷	÷	✓	÷	÷	÷	÷	Object selection of 6DoF ARM	0	0	10-16
[51]				✗		÷	÷	✓	✓	÷	÷	✓	÷	Object selection of 6DoF ARM	0	0	7
[52–55]					✗	÷	✓	✓	✓	÷	÷	÷	÷	Activation of 1DoF exoskeleton	0	6-10	5-10
[56, 57]					✗	÷	✓	✓	✓	÷	÷	✓	÷	Activating 1DoF exoskeleton	0	5	3-14
[58]					✗	÷	✓	✓	✓	✓	✓	÷	÷	1DoF control (drone)	0	0	10
[59, 60]					✗	÷	✓	÷	÷	✓	÷	✓	÷	1DoF control (telerobot)	0	9	10
[61]					✗	÷	✓	✓	✓	✓	÷	÷	÷	2DoF control (3DoF ARM)	0	0	4
[62–64]					✗	÷	✓	✓	✓	✓	✓	✓	÷	2DoF control (7DoF ARM)	0	0	5-6
[65, 66]					✗	÷	✓	✓	÷	✓	✓	✓	÷	$\leq$3DoF control (7DoF ARM)	0	0	11-13
[67]					✗	÷	✓	÷	✓	✓	✓	✓	÷	3DoF control (7DoF ARM)	0	0	15
[68]				✗	✗	÷	÷	÷	✓	✓	÷	÷	÷	5DoF control (Drone)	0	0	5
[69]				✗	✗	÷	÷	÷	✓	✓	÷	✓	÷	2DoF control (Wheelchair)	0	0	3
[70]				✗	✗	÷	÷	✓	✓	✓	÷	✓	÷	2DoF control (7DoF ARM)	0	0	5
[71]				✗	✗	÷	÷	✓	÷	✓	÷	✓	÷	3DoF control (7DoF ARM)	0	0	12
[72]				✗	✗	÷	÷	?	?	✓	÷	✓	÷	3DoF control (7DoF ARM)	0	0	10

Table 1.2: Interfaces used for robot control. The existing literature on robot interfaces using modalities available to individuals with tetraplegia. ✗ : uses modality, ✓: meets requirement, ÷: does not meet requirement, ?: not reported. ^{J}: Using jaw movements. ^{H}: Using head movements. *: Was not evaluated online.

	Modality					Usability				Control				Robot	Evaluation		
Reference	Lip/Jaw	Tongue	Eye	Evoked Brain	Spontaneous Brain	Modality adaptable	Eyes free operation	≤ 20min calibration	≤ 5 training sessions	Manual	Continuous	Asynchronous	≥ 7 DoF control	Description	ALS	Other	Healthy
[73]			✗		✗	÷	÷	✓	✓	✓	✓	✓	÷	2DoF control (5DoF ARM)	0	0	10
[74]			✗		✗	÷	÷	✓	✓	÷	÷	✓	÷	Object selection (5DoF ARM)	0	0	8
[75]			✗	✗		÷	÷	✓	✓	✓	÷	✓	÷	6DoF control (6DoF ARM)	0	0	11
[76]			✗	✗	✗	÷	÷	÷	✓	✓	÷	✓	÷	2DoF control (Wheelchair)	0	0	4
[77]			✗		✗	÷	✓	?	÷	✓	÷	÷	÷	2DoF control (Wheelchair) and object selection (7DoF ARM)	0	0	5
[78]			✗		✗	÷	✓	✓	✓	✓	÷	✓	÷	2DoF control and automated task selection (Humanoid robot or telerobot)	0	0	13
[79]			✗	✗		÷	✓	?	✓	✓	÷	✓	÷	2DoF control and automated task selection (Drone)	0	0	4
[80]			✗		✗	÷	÷	?	✓	✓	÷	✓	÷	2DoF control and automated task selection (4DoF upper limb exoskeleton)	0	4	3
[81]			✗		✗	÷	÷	?	✓	÷	÷	÷	÷	single task selection (hand exoskeleton)	0	1	5
[82–84]			✗		✗	÷	÷	✓	✓	÷	✓	✓	÷	1DoF control and task selection (5DoF upper limb exoskeleton and hand exoskeleton)	0	0-5	0-11
[85]	✗	✗				÷	✓	✓	✓	✓	✓	✓	÷	2DoF control (wheelchair)	0	0	4
[86]	✗	✗	✗			÷	✓	✓	✓	✓	÷	✓	÷	2DoF control and task selection (humanoid robot)	0	0	12
[87]	✗			✗	✗	÷	✓	✓	✓	✓	÷	÷	÷	3DoF control (4DoF ARM)	0	0	8

availability, there does not exist much research on the use of lip movements as a modality for control of an ARM.

Tongue movement-based interface

Jiang and Park presented an intraoral device that utilized optical sensors to provide four buttons based on the tongue's position in the mouth (forward, left, right, and backward) [92]. While the study only evaluated the device for planar navigation in a virtual space, it can be assumed to also allow planar navigation, e.g. wheelchair control, in the real world in the near future. Tily and Mir used an intraoral camera to distinguish 11 button outputs from different tongue positions, which they used to control a 5DoF robot arm and its end-effector [33].

The tongue drive system (TDS) was designed to use a magnetic tracer pierced to the tongue, which can be traced using magnetic sensors placed in a headset outside the mouth [93]. There was later designed an intraoral version (iTDS) of this device [94]. The TDS has been used to control wheelchairs [34]. The TDS distinguishes up to 6 buttons from different tongue positions, and has been used for controlling a wheelchair [34, 35], a rehabilitation exoskeleton with one or two DoF [36, 37].

The intraoral tongue control interface (ITCI) is one of the first developed tongue control systems (first introduced in 2006 [95]) and is still possibly the best-performing tongue control interface today. It has since been further improved and is available as a commercial product by TKS A/S for the control of computers, wheelchairs, and tablets [96]. It consists of 18 induction coils that utilize Faraday's law to measure if an "activation unit" (a metallic tongue piercing) is touching one or more of the coils [95, 97, 98]. The 18 coils are placed on two separate surfaces (10 on the anterior- and 8 on the posterior plate) and were originally designed to provide 10 buttons on the anterior plate combined with a 2-axis joystick on the posterior plate. However, later studies have applied interpolation to provide a touchpad-like functionality [99]. This allows for the design of specialized layouts with dynamic buttons, joystick-like functions and the use of gestures [27–29].

The ITCI has been used to provide control of a 4DoF upper-limb exoskeleton with one open/close functional exo-glove [29], wheelchair control [32], and is the only tongue interface to have provided 7DoF control of an ARM [27, 28, 31]. Recent studies introduce a version without the need for tongue piercings [100].

Eye movement-based interface

Eye movements have been utilized as a modality for computer control which has been made commercially available as an assistive technology through companies such as Tobii Dynavox [101]. Typical eye-tracking devices utilize infrared cameras to detect the eye pupils and the direction of gaze, to provide a 2-axis pointer. By presenting control options on a computer monitor Sunny et al. provided an HMI capable of full ARM control and control of a wheelchair [38]. Cio et al. provided semi-autonomous control of an ARM using eye-tracking without a monitor, by projecting the 2-axis pointer to a 3D position in space where objects could be detected [39]. 3D gaze estimation has also been researched and used as semi-autonomous control for the ARM [40, 102]. Eye-tracking using an optical camera does have drawbacks as it may have issues tracking certain eye types and handles disturbances caused by e.g. glasses or contact lenses [103]. As an alternative to using optical sensors to measure the eye position, it is possible to do so using an electrooculogram (EOG), which measures the corneo-retinal potential. Reynoso et al. used EOG to control the 3D trajectory of an ARM [41].

Brain signal-based interface

The use of brain signals for control modalities in HMI has been highly researched in recent years. Especially research where invasive electrodes, i.e. microelectrode arrays or electrocorticography (ECoG), have presented some impressive and hopeful results, where several individuals with tetraplegia have gained up to 10 DoF control of an ARM using only their thoughts [104–108]. While impressive, this required both a lot of training (Collinger et al. reported robust 7DoF control after 13 weeks of training [109]) and a not risk-free operation. To avoid the need for surgical procedures many researchers are looking to non-invasive methods of recording brain signals, such as electroencephalogram (EEG) [110]. EEG-based HMI, hereafter referred to as brain-machine interfaces (BMI), can be divided into one of three categories based on the type of brain activity used: (1) spontaneous brain signals, which are voluntarily generated by the user; (2) evoked brain signals, which is generated by outside stimuli; or (3) a hybrid of both spontaneous and evoked brain signals [110].

Movement-related brain activity is the most common spontaneous brain signal used for BMIs. They have been used for simple activations of hand/upper-limb-exoskeletons [52–57], planar navigation of robots (such as wheelchairs) [58,59,111–115], or planar navigation of a robot end-effector [61–66]. Using a constant forward velocity, it is possible to control a quadcopter in a virtual- and real 3-dimensional space [116,117]. Jeong et al. classified imagined 3D movements of an arm and used these to control the position of an ARM, with a success rate of 66% in reach-and-grasp tasks [67]. However, these systems require long calibration/training sessions (Jeong et al. reported a necessary 3-4 hours at every setup [67]) and it has not yet been possible to achieve more than 3DoF control of a robot-arm [118].

Evoked brain signals are typically generated using visual stimuli. Blinking lights or moving images will generate visually evoked potentials (VEP) when attended to. Depending on the stimulation design these signals can be e.g. event-related potentials (ERP) using odd-ball paradigms, steady-state VEP (SSVEP) using fixed frequency stimulations, or code-modulated VEP (c-VEP) using pseudorandomized stimulation [119–123]. As this requires the visual attention of the user it is comparable to eye-movement technologies [124], though VEP-based BMIs can also be used without the dependency of eye-movement (but with much lower performance) [125–128]. SSVEP and c-VEP allow several uniquely modulated stimuli to appear simultaneously, which allows a high number of classes that the user can select. It is therefore often developed for keyboard applications with a high information transfer rate (ITR) [129–132]. With more classes and a higher signal-to-noise ratio compared to spontaneous brain signals, VEP-based BMIs have also achieved better performance with control of robots, such as wheelchairs [42,43,48,133], a hand prosthesis [47], autonomous control of an ARM or upper-limb exo [49–51, 134], spatial control of a mobile robot arm [45], planar control and grasping with a humanoid robot [44], or even discrete manual control of an ARM [46]. While the BMI developed by Chen et al. provided 6DoF control of a robot, it was synchronous (the brain signals are only analyzed in predefined windows [135]) and discrete in time (i.e. the user could only control the robot in incremental steps, which was synchronized to the robot and not the user) [46]. It has not yet been possible to provide full control of an ARM (where the control is also asynchronous and continuous in time) using a VEP-based BMI.

Spontaneous and evoked brain signals can be used in combination and have been used to planar (wheelchair or virtual) control [69, 136–138], spatial control of a quadcopter [68], or navigation and autonomous object selection with a humanoid robot [139]. Some hybrid BMIs further utilize a brain signal called error-related potential (ErRP), which occurs when humans observe errors to correct errors made while controlling the robot and have been utilized to provide control of up to 3-axis on a robot arm [70–72].

Multimodal interface

Similar to a hybrid BMI, a multimodal or hybrid HMI utilizes two or more modalities to improve the performance of the system [26, 140].

Especially eye-movement/blinking and brain signals have often been coupled for a hybrid BMI for semi-autonomous or manual control a 5DoF robotic arm with gripper [49,73,74], a wheelchair [76], a wheelchair with autonomous ARM control [77], a humanoid robot [78], spatial control of a quadcopter [79], and control of upper limb exoskeletons [80–84]. Tongue movements have been combined with jaw movements to control of wheelchair [85], and have also been combined with both jaw- and eye-movement to control a humanoid robot [86]. Jaw movements have been combined with brain signals to allow incremental position control of a robot arm [87]. Individuals with less severe tetraplegia may have some functionality of shoulder and/or neck muscles and are used to control a robot arm [141]. These modalities have also been combined with eye movements [142, 143] or tongue movements [144].

With the TOBI project, Müller-Putz and his team worked on a multimodal HMI framework concept following a similar idea, with a focus on combining brain-machine interfaces (BMIs) with other modalities [140]. Similarly, previous studies have proposed HMI frameworks, where the users can select their preferred single-modality control method from a sub-set of modality choices (e.g. brain control or tongue control), to better tailor the system to the user's preference and mobility [144–146]. While the HMI frameworks could be considered a multimodal HMI (as they provide control through multiple modalities) the modalities were used independently of each other and not used to improve performance: only to tailor the system to the users' preferences. However, the tailoring is still limited, as the user must select a single modality for control. Therefore, this thesis developed a multimodal HMI framework.

1.4 A multimodal-framework

As ALS causes progressive paralysis, the individuals suffering from the disease will likely rely on different modalities for their HMI throughout the disease, which has been reported to cause bureaucratic issues (e.g. insufficient availability of assistive devices) [147–150]. It is furthermore not ideal that the user must relearn to use entirely new systems when an "old" modality is no longer fully functional because of the disease progression. It could therefore be beneficial to develop a multimodal HMI framework for full control of an ARM, that individuals with ALS can use efficiently in all stages of their disease.

In the early stages of the disease, the individual with ALS may use muscular functionalities below the neck e.g. through a joystick or electromyography (EMG). When they can no longer utilize these modalities, the user can control the ARM through muscular functionalities above the neck, e.g. jaw movement, sip-and-puff, eye tracking, or tongue control. As tongue machine interfaces (TMI) have been shown to allow full, continuous, and eyes-free control of an ARM this modality is considered the optimal choice.

However, as ALS will eventually also affect the bulbar muscles, individuals with the disease may eventually only have brain signals left as a functional control modality. Therefore, a control method that gradually changes from efficient tongue control to brain control is desirable. Thus, this thesis describes the research on- and development of a multimodal HMI, that can be adjusted to the progression of ALS and facilitate a gradual transition of the individual from using tongue movements to using non-invasive brain signals for full 7DoF control of an ARM. The resulting framework included full 7DoF control of an ARM using only brain signals, which had not yet been accomplished. Based on existing literature, it was deemed more realistic to create such a BMI using evoked SSVEP signals, rather than spontaneous signals. However, we also investigated the possibility of using spontaneous signals.

Chapter 2. Aims and Objectives

This Ph.D. project investigated the feasibility and advantages of a hybrid tongue-brain robot interface framework, designed for individuals with ALS to allow for the adaptation of the interface to the progression of the paralysis. The interface framework was designed for time-continuous direct cartesian control of a 7DoF ARM. The thesis project had the following four objectives:

A) Design and development of a framework for a shared tongue-brain control interface:
How should the user efficiently transition from a full tongue control interface to a full SSVEP-based brain control interface? How should brain control signals complement and later replace tongue control signals without greatly diminishing control performance? The framework requires research on several novel topics. A multimodal tongue-brain control interface was in itself a novel technology. Integrating it as a framework that gradually changes from tongue-based control to brain-based control further imposes complexity. It was necessary to ensure a logical transition between the gradual modality changes and to ensure that 7DoF ARM control was possible regardless of the selected combination of shared modality control (including full tongue or full brain control).

B) Implementation and experimental evaluation of the framework:
The developed framework creates a platform for gradually changing from tongue-based control to brain-based control through adapted shared control between the two modalities. The effect of this has not previously been studied, thus this objective focus on such an experimental study. It will provide important information and feedback from healthy users and clinical case studies to further improve the framework.

C) Clinical evaluation of the updated hybrid framework:
Upon improving the framework a clinical evaluation should be made, to better evaluate the effect for potential end-users. The improved framework will be tested and evaluated with individuals suffering from ALS. This will evaluate the usability of the systems for individuals with decreased motor functionality and provide valuable feedback from potential end-users.

D) Investigation of brain signals generated through tongue movements for a direct tongue-to-brain transition:
As completely locked-in patients may have difficulties using SSVEP-based BMI, a secondary study will investigate the potential of directly

replacing the TMI with an MRCP-based BMI. This will be especially beneficial for individuals in a completely locked-in stage, as they may not have the capability of using an SSVEP-based BMI.

2.1 Dissertation overview

This thesis presents the development and evaluation of a tongue-brain control interface framework designed for individuals with ALS to allow full control of a 7DoF assistive robot, which can be adapted to the progression of the paralysis, by sequentially decreasing the use of the tongue modality and increasing the use of the brain modality.

Chapter 3 will present the algorithm developed for the hybrid framework and present the results of pilot studies made for early developments and evaluations of the framework. Chapter 4 will provide a summary of the main studies for this PhD thesis which are:

Study I. Adapting to progressive paralysis: A tongue-brain hybrid robot interface for individuals with amyotrophic lateral sclerosis
This study presents the development and experimental evaluation of the first framework design, which was tested with healthy individuals and three individuals with ALS at different stages of the disease (following aims A and B).

Study II. Evaluation of an adaptive hybrid tongue-brain control framework by individuals with amyotrophic lateral sclerosis
Following the experience gained from study II, this study will evaluate an improved framework with three individuals with ALS (following aim C).

Study III. Feature- and classification analysis for detection and classification of tongue movements from single-trial pre-movement EEG
This study evaluates the detection and classification of tongue movement using EEG to investigate the possibility of a tongue-to-brain control framework that can utilize the intention of tongue movements when physical movement is no longer possible (following aim D).

The thesis is concluded in chapter 5 where the main findings and the future perspectives are discussed.

Chapter 3. Design and Implementation of the Hybrid Framework

The framework consists of sub-systems consisting of various modality combinations of tongue and brain control. This chapter will first describe the development of the single modality tongue HMI (the TMI), then the single modality brain HMI (the BMI), and then the hybrid sub-systems that combine the two modalities (the TBhMI).

3.1 Inductive Tongue Machine Interface

The inductive tongue computer interface (ITCI) is an intraoral TMI device, mounted at the hard part of the intraoral palate with a brace (very similar to a standard dental retainer). It consists of 18 inductive coils on two 10-layer PCBs, one anterior board with 10 coils and one posterior board with 8 coils, which can be activated by placing a metallic unit - an activation unit (AU) - over the coils [151]. The AU is typically fixed as a tongue piercing but is simply a titanium piece glued to the participant's tongue within the experiments of this thesis. The change of inductance across each coil is used to determine the level of activation. Using the nearest neighbor algorithm, the position of the AU on the ITCI surface can be derived [99, 152, 153], which can then be used within a control interface. As the control signal after signal processing is a 2-dimensional pointer it allows for a very customizable

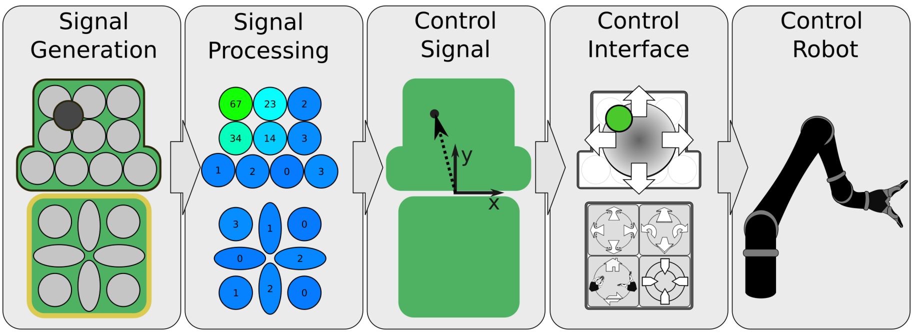

Fig. 3.1: The process of generating a control command by the ITCI. The user may activate coils on the ITCI surfaces, by placing an AU on the area (here shown as a dark circle). The level of activation is calculated from the inductance measured across each could. Using the nearest neighbor algorithm a control signal consisting of an XY-coordinate of the AU is calculated. The XY-coordinate is used with the control interface to determine the control command which is then sent to the robot while the signal remains active.

interface, wherein areas of the ITCI surfaces can be separated into joystick or buttons. Fig. 3.1 exemplifies the processes used from activating the coils to creating a control command for the robot. The interface in this example uses a 2-axis joystick on the anterior surface combined with 4 buttons on the posterior. Thus, if users with limited tongue movement have issues hitting e.g. a small button on the ITCI, the software can simply be reprogrammed to have bigger buttons, although this will consequently also result in fewer buttons (as the surface area of the ITCI is fixed).

3.2 Steady State Visually Evoked Brain Machine Interface

As previously stated, SSVEP is among the highest-performing non-invasive brain signals for BMIs. It requires multiple visual stimuli flashing at unique frequencies and/or phases, presented either on a computer monitor or external hardware (e.g. LED arrays). Figure 3.2 exemplifies how the SSVEP-based BMI was used to control an ARM. This thesis implemented the stimuli using a computer monitor, where up to 16 dedicated areas provided unique visual stimuli that could be classified from EEG. The EEG was mainly recorded from the occipital lobe using passive wet electrodes and the OpenBCI Cyton board [154]. The classifier was developed to provide an "activation value" for each stimulus, indicating the estimated probability of the user attending to the specific stimulus. While an activation value exceeds a predefined threshold and all other activation values are below, the button assigned to this stimulus is considered active. This allows for a control interface with up to 16 buttons that the user can activate through visual attention. Each button can then be assigned a corresponding control command (e.g. move left) that the robot can perform while the button is activated. An early pilot study made during this PhD evaluated four design strategies to evaluate different stimuli designs for a 60Hz computer monitor and investigate two aspects [155]:

1. **Is there a benefit to using stimulation frequencies that resonate with the monitor refresh rate?** The pilot study did not show an advantage of using resonating frequencies. In fact, the designs using non-resonating frequencies were generally higher than those using resonating frequencies. This was expected, as the stimuli were designed to be sampled sinusoidal proposed by Manyakov et al. [156], and it allowed an evenly divided set of frequencies.

2. **Is it better to have four, eight, or sixteen unique frequencies combined with 16 unique phases?** This seemed to be partly user-dependent; however, all designs achieved high performance. Importantly, it showed that different stimuli used to generate SSVEP can have the same frequency and still be distinguished if the stimuli have different phases.

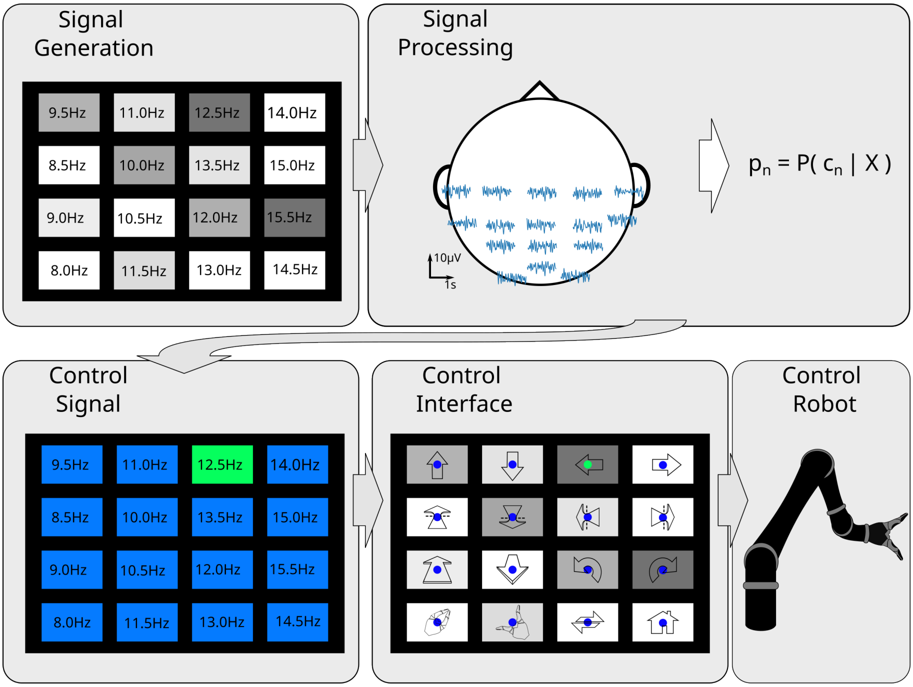

Fig. 3.2: The process of generating a control command by the BMI. The user may gaze at one of the multiple dedicated areas (buttons) on a computer monitor, each flashing with specific frequencies. For each unique simulating frequency, the probability of it being gazed upon is then estimated from EEG signals and a trained machine-learning algorithm. If one and only one of the estimated probabilities exceeds a threshold, the button flashing with this frequency is recognized as active and the button's allocated control command is sent to the robot while the button remains active.

To classify the EEG signals, the pilot study also implemented an improved version of an existing SSVEP classifier: the spatiotemporal beamformer (STBF) [155]. The STBF was first introduced by Wittevrongel and Van Hulle [157] as an improvement to the stimulus-locked inter-trace correlation (SLIC) method [158]. Other SSVEP classifiers, including the high-performing Task-Related Component Analysis (TRCA) [131, 159] and the popular canonical correlation analysis (CCA) [130, 160] have been improved using a filter bank (FB) that focus on also classifying higher resonating frequencies to the stimulation frequency. Therefore a FB-STBF was designed to improve performance [155].

While existing SSVEP-based BMIs are designed to provide synchronous triggers (i.e. the machine asks "what action do you want" and the user then triggers a desired action) it was believed that an asynchronous button could be achieved (i.e. the human push the action and the machine perform this action until the human releases the button). However, this would require a classification algorithm to calculate the activation status of each button at a high rate with low computational delay and with high accuracy. Therefore, the classifier was further improved with a focus on reducing the required computing power in our later study [161]. Here a new version of the TRCA was also developed (the SLIC-TRCA) by implementing the SLIC method (similar to the STBF). The study showed the greatest advantage of classifiers using the SLIC method, as it can split the computations into smaller time segments and become independent of the classification time window. In the study, it was shown to reduce the maximum computational delay time was reduced from 0.33ms to 0.03ms [161]. The study also showed that the previously designed FB-STBF achieved a similar performance but with a slightly higher computational delay (0.07ms). While the time reduction may seem negligible, it is especially beneficial for systems with low computational power (i.e. using microprocessors) or when the computer should also handle other processes (such as stimuli generation and robot control). To select a good compromise between performance and computational costs, an STBF programmed to utilize the SLIC algorithm was therefore used for the real-time robot control experiments within this thesis.

3.3 Tongue-Brain Hybrid Machine Interface

As ALS progresses the bulbar functionality will decrease which will affect the tongue's fine motor skills (precision) and reachable workspace (flexibility). We, therefore, expected that some areas of the ITCI surface would become difficult/impossible to reach for individuals with late-stage ALS and that spatial accuracy within the reachable area would decrease. Fig 3.3 exemplify how the loss of tongue flexibility or precision may affect how a button-designed tongue interface may be designed. Loss of tongue precision will cause difficulties in accurately hitting small areas on the ITCI, while a loss of tongue flexibility will reduce the range of motion the tongue can reach and therefore the usable surface area of the ITCI. While the effect of bulbar symptoms has not been investigated, previous studies have shown that anterior areas of the ITCI achieve higher throughputs for healthy participants [169]. It has therefore been assumed that the posterior areas would be more affected by reduced tongue functionality. Regardless of how it will impact the ITCI usability the effect of reduced tongue functionality is a reduction of control signals.

The robot control requires the same number of control signals regardless of the loss of tongue-based control signals, brain control signals can be implemented as a secondary control signal. Fig 3.4 illustrates two methods of doing so that were considered:

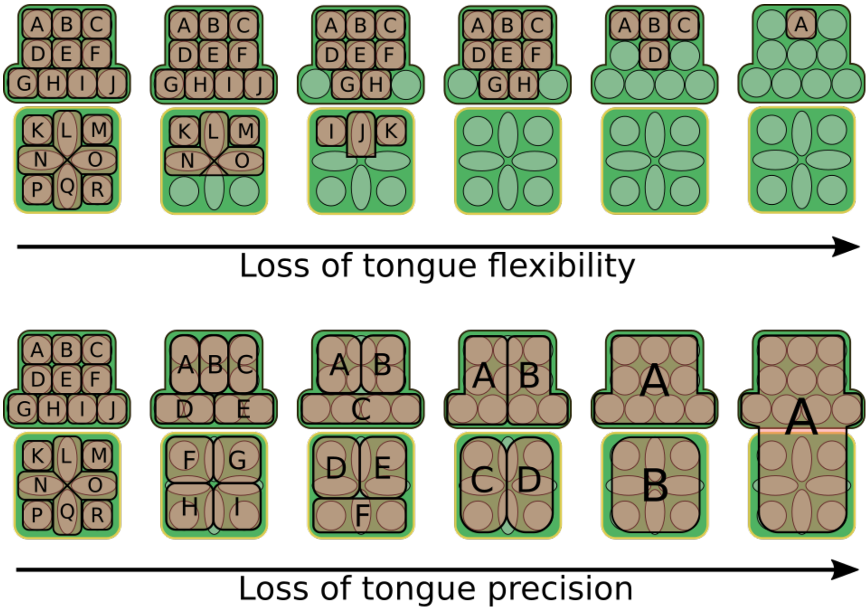

Fig. 3.3: An exemplification of usability of the ITCI after the loss of tongue movement precision and/or functionality.

> **Method A - Parallel connection**: Where the brain and tongue interface are used simultaneously. E.g., the tongue can send a "left" command while the brain sends a "forward" command.
>
> **Method B - Series connection**: Where the brain and tongue interface are used sequentially. E.g., the brain selects which command the tongue should access.

While the parallel connection can provide the user immediate access to all control commands, the series requires two steps: first selecting a *control mode* using the BMI and then controlling the robot within this mode using the ITCI. Thus, the parallel connection is considered to have a higher potential for control performance, but it is also considered to be more complicated for the user as they will need to remember how the control commands are mapped to the modalities. Furthermore, as the BMI will have a weaker control signal compared to the ITCI, the control commands mapped to this modality will be more difficult to activate compared to those mapped to the tongue. The series connection will use tongue control as the final and continuous control command regardless of what that command is, which will ensure that all commands are equally easy to select and use. Furthermore, it will allow the user to have a visual focus on the robot, regardless of which control command they use. For these reasons, a series combination was used in this thesis.

3.4 Robot Arm Control System

The overall system setup is illustrated in figure 3.5. It was designed to allow cartesian velocity control of the robot arm, control the robotic gripper closure, and allow a home command for the robot. The robot control software was programmed within the Robot Operating System (ROS) framework and is running on a Lenovo T480 laptop. There are several hardware components connected to this main laptop.

The ITCI mouthpiece unit (MPU) is placed in the palate of the user's mouth, where they can activate the coils using an activation unit (AU). The MPU wirelessly sends the coil activation levels to a central unit (CU) that is connected via USB to the main laptop. Brain signals are measured using EEG recorded via Ag/AgCl passive electrodes connected to the OpenBCI Cyton board. Also connected to the OpenBCI cyton board, is a photoresistor that records a trigger indicating when the visual stimuli are active. The EEG data and trigger is transmitted to the main laptop using WiFi. The visual stimuli are presented on an external computer monitor connected to the laptop with an HDMI cable. Lastly, the robot arm is connected to the laptop using USB.

3.5 Tongue Brain Machine Interface

The developed robot arm control system provides full tongue, tongue-brain hybrid, and full brain control of an ARM, which will allow individuals with ALS to use the system independently of their remaining tongue functionality. When the system becomes available, the individual may therefore use this

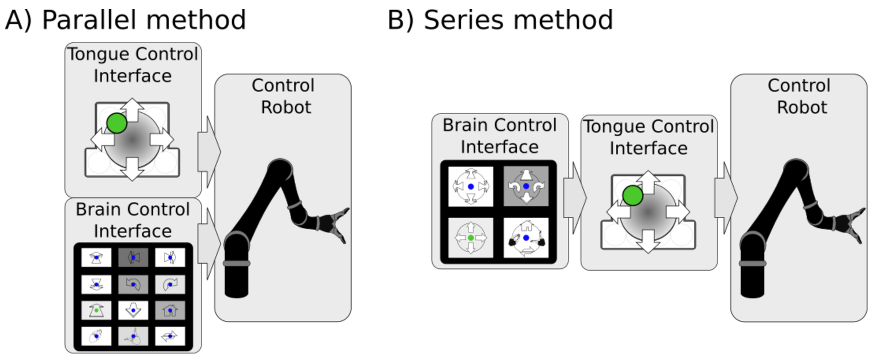

Fig. 3.4: Two multimodal methods for combining brain and tongue control: (A) a parallel connection and (B) a series connection.

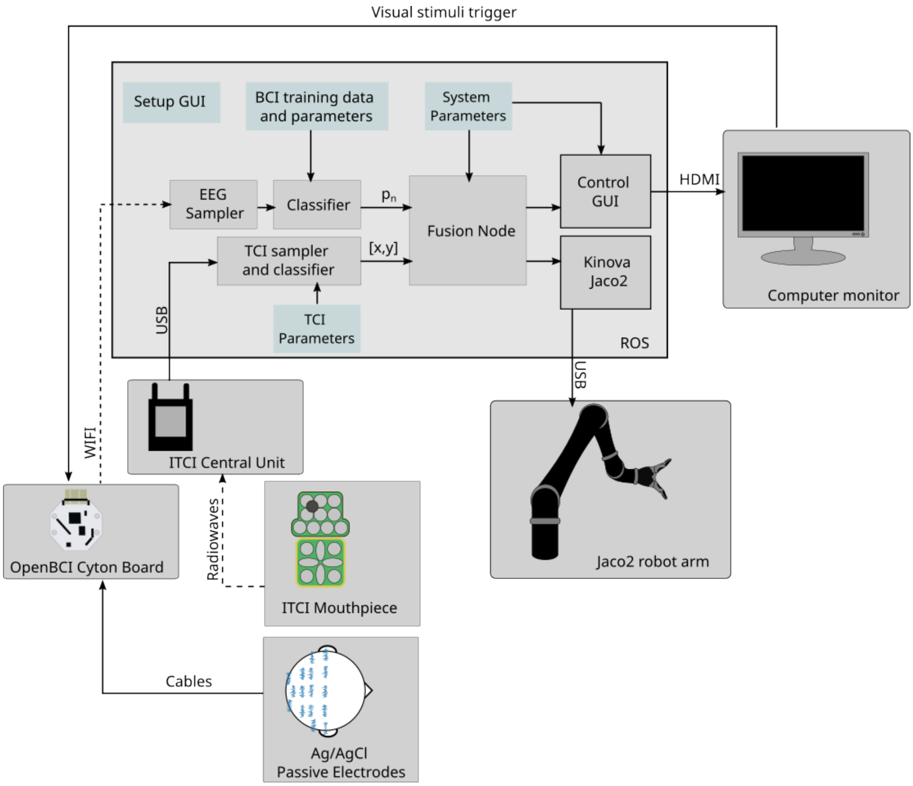

Fig. 3.5: The overall multimodal robot control system

system for a longer time compared to a typical interface for individuals with ALS. This is greatly beneficial to the user, and may also be beneficial for a scientist as the recorded EEG could also be utilized to further improve the control interface or to monitor the disease progression.

It is hoped that during months of recording both tongue movement and brain signals, we may generate enough user-tailored data to map the user's specific brain signals when executing complex tongue movements. If this is possible, we may also detect when it is attempted to perform complex tongue movements, even in late-stage ALS when no tongue movement functionality remains. If so, this could be used as a motor imagery-based BMI.

Executed movements and imagined movements generate similar brain signals and can be measured seconds before the actual movement as movement-related cortical potential (MRCP) [163]. Thus, EEG recorded before the tongue movement execution may be used to detect and classify the intended tongue movement. This is especially beneficial for this system design, as we desire to use data generated from actual movement to classify intended movements (when the user can no longer move their tongue). By focusing on data prior to the actual tongue movement, it will not include possible disturbances generated by the actual movement (such as the glossokinetic potential or contact between the tongue and ITCI). In a pilot study, we showed that MRCP appear in the EEG when individuals with ALS used the ITCI for control and that the ITCI can efficiently be used to synchronize when the movement occurred across multiple trials [164].

However, complex movement tongue movements are very rarely investigated in BMI, even with data sampled in perfect and controlled conditions. Therefore we first investigated the possibility of detecting complex tongue movement in laboratory conditions. An early investigation showed that cued tongue movements could be detected in healthy participants, with an accuracy of 79.79% [165]. Furthermore, this study showed that classification using a common spatial pattern (CSP) algorithm could classify between left and right tongue movements with an accuracy of 71%, between Left, Up, and Right movements with 55% and between Left, Right, Up, and Down movements with 41% accuracy. Importantly, this study only used data recorded prior to the movement occurring, such as the movement-related cortical potential (MRCP) [163], as illustrated in figure 3.6. However, the CSP is more typically used with signals generated after the movement. Therefore, we investigated alternative algorithms for the detection and classification of movement before the movement execution in Study III.

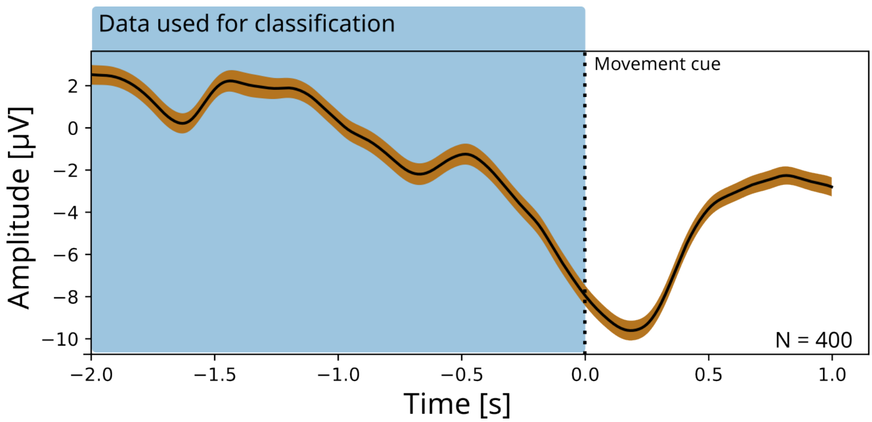

Fig. 3.6: The average MRCP measured at Cz across 400 trials for one subject performing a tongue movement cued at t = 0s

Chapter 4. Thesis experimental studies and findings

This chapter will present a summary of the three main experimental studies made of this Ph.D. thesis. Study I developed and evaluated the first versions of the developed adaptive tongue-brain machine interfaces for full control of a 7DoF arm and evaluate the system with 10 healthy participants and three individuals with ALS. Study II develop an improved framework and evaluate it with three new individuals with ALS. Study III investigates the possibility of detecting and classifying complex tongue movements with 10 healthy participants.

4.1 Study I

Title: Adapting to progressive paralysis: A tongue-brain hybrid robot interface for individuals with amyotrophic lateral sclerosis

Authors: Rasmus Leck Kæseler, Dario Farina, Bo Bentsen, Izabella Obál, Lotte Vinge, Kim Dremstrup, Mads Jochumsen, and Lotte N S Andreasen Struijk

Journal: Submitted to Computers in Biology and Medicine, preprint at TechRxiv doi: 10.36227/techrxiv.21975476.v1

Study I developed and evaluated the first versions of the developed adaptive tongue brain-machine interfaces for full control of a 7DoF arm. The framework consisted of six subsystems (subsystem A-F) with varying weights of tongue and brain control to provide time-continuous access to 16 control commands. Subsystem F was the first non-invasive full BMI system to provide full time-continuous control of a 7DoF ARM and the framework presented the first multimodal control framework designed to adapt to ALS progression. The framework was first tested with 10 healthy participants to identify the benchmark performance of each subsystem relative to the weight of tongue versus brain control used in each subsystem. Following the observations made during these experiments, small improvements were made to the framework and it was evaluated with three individuals with ALS.

The framework was developed as six subsystems as illustrated in figure 4.1. Subsystem A used only tongue control by allocating 16 of the 18 coils in the ITCI as control buttons. Subsystem B-E used tongue brain hybrid control in a series method design (see fig. 3.4), where the BMI was used to select a control mode and the ITCI was used to control the robot within the selected mode. By increasing the number of control modes between each subsystem, there would be an increased number of BMI-selectable commands while the number of ITCI commands needed within the control mode would decrease. Thus, subsystem B had a mode selection with two control modes that could be selected using an SSVEP-based BMI, and within the selected control mode the user could select eight control commands using the ITCI. With subsystem E the user could select between 16 different control modes using the BMI and within a selected control mode the user could activate only one control command using the ITCI.

The experiments with healthy participants were made over three consecutive days to also evaluate the effect of training with the systems. Each day the participant tested the six subsystems in random order, wherein each test consisted of four successful trials controlling the ARM using the subsystems. In each trial, the participant should control the ARM to reach and grasp a bottle of water, move the bottle to an empty glass and pour water into the glass. Figure 4.2 shows the average completion time spend to complete the trials using each subsystem. It was observed that the full BMI (subsystem F) was much slower than the full ITCI (258s versus 86s on the third day). The hybrid systems got gradually slower with task completion times of 113s,

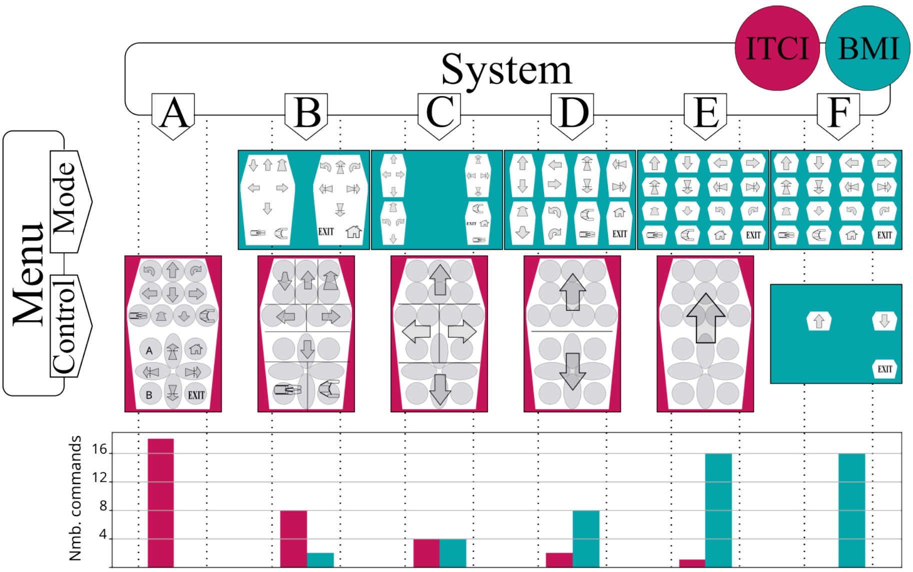

Fig. 4.1: The six subsystems used in the framework that was evaluated with healthy participants in study I (adapted from [166])

121s, 141s, and 147s for subsystems B, C, D, and E, respectively. It was also observed that much more errors occurred with subsystem F versus the other systems. It was concluded that the considerable decrease in performance with the full BMI was caused by a reduced time-continuous control signal quality. Subsystem E used the ITCI only as a time-continuous activation signal, which caused much less time spend idle in a control mode compared to subsystem F where the time-continuous activation was generated as a BMI signal by continuously focusing on the desired visual stimulus. The BMI targets were difficult to properly activate for longer periods and accurately deactivate when intended. Furthermore, its need for visual attention reduced the visual overview of the trajectory of the robot.

Thus, the experiment with healthy participants showed a great advantage of utilizing any remaining tongue functionality in combination with a BMI.

The case studies with individuals with ALS were conducted over two days. On day one the participant tried all subsystems and it was identified which of the hybrid subsystems was best suited. On day two the participant performed three trials with the best-suited hybrid subsystem (B, C, D, or E), the full ITCI (A) and the full BMI (F). In each trial, the participant was asked to reach and grasp a bottle, and then send the robot to its home position using a "home"-command available in all subsystems. Slight changes were made to the subsystems based on the observations with healthy participants. The most significant changes were:

- Previously the use of double-clicks on the ITCI had been used to switch from control mode to mode selection; however, that had shown problematic performance during the experiments with healthy participants. It was therefore replaced by an SSVEP-BMI command that could be accessed while in the control mode.
- Reaching the most distal areas of the ITCI was observed to be the most difficult, though all healthy participants were able to. However, it was chosen to design the hybrid systems using only the anterior surface of the ITCI, as a greater loss of tongue flexibility was expected in individuals diagnosed with ALS.

Two of the three individuals with ALS, who tested the framework in study I, had very minor bulbar symptoms and were able to use all subsystems, while the last had no remaining tongue functionality and could only use the full BMI.

The first participant experienced difficulties reaching the distal areas of the ITCI on the first day of trials and reported subsystem B as his favorite. On day two he could reach the distal areas, but still performed slightly better with subsystem B than subsystem A (with 40s and 44s average task completion time, respectively); however, he reported subsystem A as his favorite

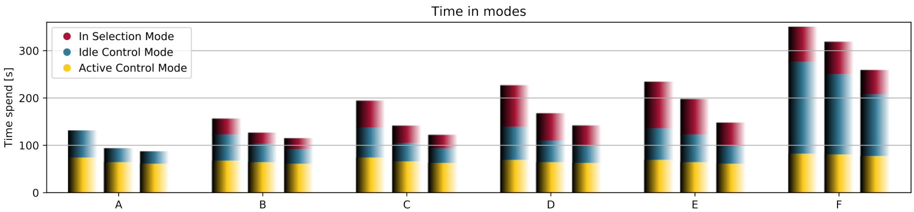

Fig. 4.2: The six subsystems (A-F) used in the framework that was evaluated with healthy participants in study I. The bar plots show the average time spend across the four trials and ten subjects on days 1 to 3 (from left to right) for each subsystem. (adapted from [166])

on day two. The second participant performed better with the full BMI, but worse with full ITCI and hybrid subsystem compared to participant one. While he achieved the shortest average task completion time with the full ITCI (100s versus 208s for the full BMI), he reported the full BMI as his favorite subsystem. The last participant was unable to use any tongue functionality and therefore only tried the full BMI (subsystem F). While she was able to gain control of the robot on the first day (completing the trial once in 414s), she was unable to complete any trials on the second day. It was believed this unsuccessful online performance was caused by fatigue and a lack of training with the robot.

Thus, this study showed the advantage of combining remaining tongue control with brain control, if the tongue control can no longer be fully utilized. The experiments with healthy participants showed that a direct transition from tongue to brain control would cause an increased task completion time of 200%, but that the proposed hybrid subsystems would instead cause a stepwise increase between subsystems of 4-32%. However, this study also identified several points where the framework may be improved such as implementing more visual feedback and reducing visual fatigue.

4.2 Study II

Title: Evaluation of an adaptive hybrid tongue-brain control framework by individuals with amyotrophic lateral sclerosis

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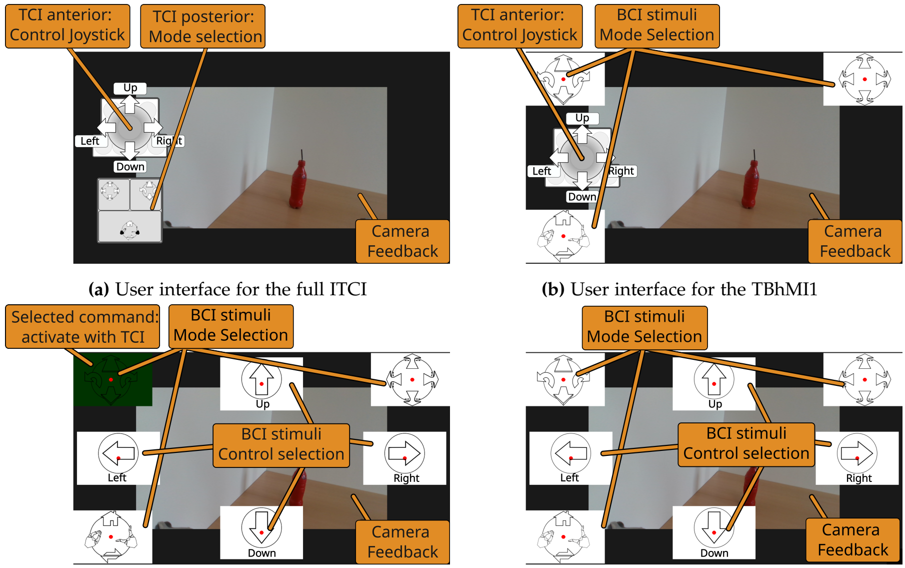
Following study I, several points of improvement were identified; therefore, study II was made to develop the framework further. It was then evaluated with three individuals with ALS, who had not previously tried multimodal control of an ARM. The developed framework consisted of four sub-systems, which all shared two design choices: visual feedback from the ARMs end-effector was presented at the center of the screen and a control layout consisting of four control modes with four control commands each.

The four subsystems are illustrated in fig. 4.3 and were:

- **The full ITCI (fig. 4.3a)** was designed using a joystick layout on the anterior MPU surface. This had previously been shown advantageous compared to a button design used in study I [28]. The distal plate was then used to select the desired control mode.
- **The first hybrid (TBhMI1, fig. 4.3b)** also used a joystick layout on the anterior MPU surface but did not use the distal surface (as study I showed this area is difficult to reach for some users). Instead, the control mode could be selected using SSVEP-based BMI, where the three unused control modes were presented as stimuli at the corners of the screen. The stimuli were designed to only activate when the ITCI was not in use to reduce fatigue.
- **The second hybrid (TBhMI2, fig. 4.3c)** used only the ITCI as an activation button. The four control commands were therefore presented as BMI stimuli at the sides of the screen. Thus, the user could select one of the four control commands or one of the three mode-switching commands using the BMI; hereafter, the selected command would be presented as dark green. Upon activating the ITCI the selected command would activate and turn light green.
- **The full BMI (fig. 4.3d)** was designed similarly to the TBhMI2; however, to activate any of the commands in this subsystem the user should only remain focused on the blinking stimulus.



(a) User interface for the full ITCI

(b) User interface for the TBhMI1

(c) User interface for the TBhMI2

(d) User interface for the full BMI

Fig. 4.3: The user interfaces for the four sub-systems used in study II (adapted from [167]). Orange labels were not shown on the interfaces but were added here to provide descriptions of the interface components.

Other hardware improvements were made to the system. A camera was mounted on the end-effector to allow visual feedback. Eight additional electrodes were implemented in the EEG headset (for a total of 16 electrodes), to improve the BMI performance. The ITCI MPU was fastened using a user-tailored dental sheet to reduce its size and increase comfortability. Lastly, the monitor used for visual feedback was upgraded to a portable monitor with a high refresh rate (240Hz). Being portable would allow it to be easily mounted on a wheelchair and used away from power supplies, but more importantly: the high refresh rate would reduce visual fatigue.

The updated framework was evaluated with three individuals diagnosed with ALS. The experiment was conducted over three days where the first day was used to introduce the full ITCI and the full BMI control, on the second and third day the participant tried all four subsystems to complete a trial three times. In the trial, the participant was asked to reach and grasp a bottle and then send the robot to its home position, similar to the trial of study I. The three participants' task completion times for the successful trials on day three are shown in fig. 4.4.

The first participant had some issues hitting the distal plate of the MPU and was unable to complete any trials with the full ITCI on the second day. On the third day, he was able to complete three trials using the full ITCI,

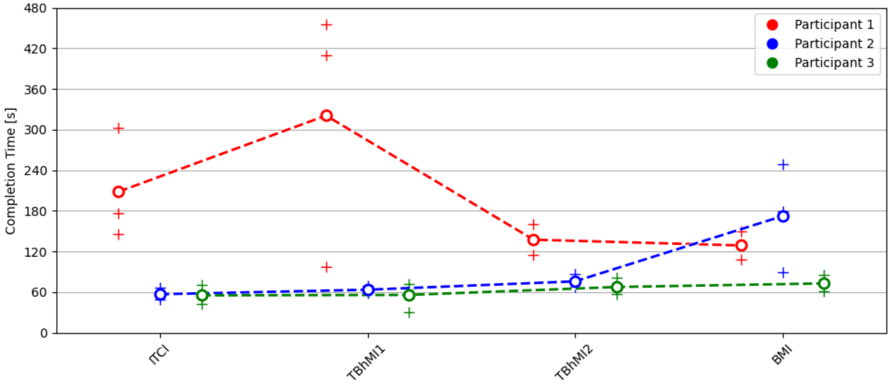


Fig. 4.4: The task completion time for successful trials with three ALS diagnosed participants (P1-P3) in study II (adapted from [167]). The successful trial times are presented as plus signs while the circles show the average of the successful trials. Participant P1 was unsuccessful in one TBhCI2 trial and one BMI trial. The other participants were successful in all trials.

but achieved the best trial time using the TBhMI1. However, the average completion times with the ITCI and TBhMI1 were fairly high (208s and 254s, respectively). While he had one incomplete trial with both the TBhMI2 and the full BMI, he achieved the best average completion time with these systems (137.5s and 129s, respectively). He chose the TBhMI2 as his favorite subsystem.

Participants two and three both had good control using the full ITCI, and very similar control with the TBhMI1. Participant two chose the TBhMI2 as her favorite subsystem, while the third participant chose the TBhMI1. Participant three achieved excellent performance with all four subsystems with an average task completion time of 55s, 56s, 68s, and 73s for the full ITCI, TBhMI1, TBhMI2, and full BMI, respectively. Participant two achieved similar times for the full ITCI and the hybrid systems, but a much higher time with the full BMI (172s).

Still, all three participants achieved better performance using the full BMI compared to the full BMI of *study 1*. This is likely because of the implemented camera feedback and improved control strategy. The ITCI performed similarly to that of *study 1*; however, evaluation of the framework performance over the last two days indicated that the participants were still learning to use the ITCI to its fullest. The transition between subsystems included stepwise performance drops compared to *study 1*, indicating a better transition between subsystems.

While the study had few participants it further illustrated the advantage of multimodal control. Importantly, all participants chose a hybrid subsystem as their favorite and all participants indicated a good acceptance of the framework. All participants were able to utilize all subsystems within the framework and provided only small suggestions for changes. The first participant showed that not all individuals can utilize the ITCI to its fullest, but that remaining tongue functionality can still be used beneficially. The second and third participants showed that even with great tongue functionality some users may prefer the inclusion of BMI control.

4.3 Study III

Title: Feature and Classification Analysis for Detection and Classification of Tongue Movements From Single-Trial Pre-Movement EEG

Authors: Rasmus Leck Kæseler, Tim Warburg Johansson, Lotte N S Andreasen Struijk and Mads Jochumsen

Journal: IEEE Transactions on Neural Systems and Rehabilitation Engineering, vol. 30, pp. 678-687, 2022, doi: 10.1109/TNSRE.2022.3157959.

A major advantage of using a BMI in the adaptive framework is that it will allow long-term recording of EEG that may be used for monitoring ALS and/or calibrating a BMI to better fit the user. Here spontaneous EEG signals were considered especially interesting, as it would allow a control signal even if the participant is in a complete locked-in stage. The ideal adaptive framework would utilize remaining tongue functionality, as described in study I and II while saving the EEG epochs when tongue movements were identified. The system could then passively calibrate a tongue movement based-BMI, that would eventually allow detection and classification of complex tongue movements and thus replace the ITCI when the user no longer has sufficient tongue functionality.

However, as there existed no studies on the classification of complex tongue movements, it was uncertain how possible such a system would be. Therefore, this study investigated the brain activity of ten healthy participants performing complex tongue movements to evaluate the feasibility of a tongue-movement-based BMI. Four types of tongue movements were investigated: left, right, upwards, and downwards as illustrated in fig. 4.5,

The 10 participants performed 400 cued tongue movements: 100 movements "up", "down", "left", and "right". The cues were designed to record MRCPs and only use pre-movement EEG, as the glossokinetic potentials that occur when the tongue makes contact were assumed to create disturbances.

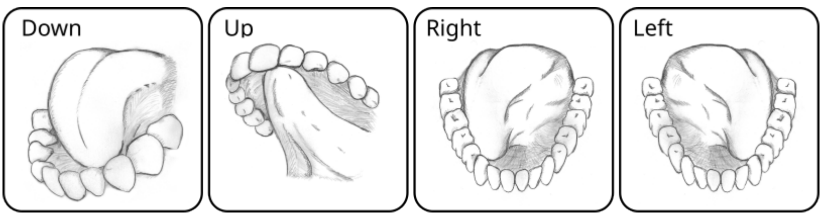


Fig. 4.5: Illustraion of the four tongue movements performed in the experiments for study III (adapted from [168]).

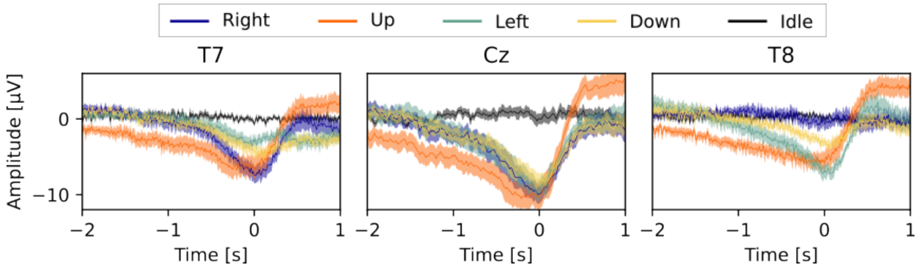


Fig. 4.6: The average MRCP of the four-movement types recorded at T7 (near the left ear), Cz (top of the head), and T8 (near the right ear). (adapted from [168])

The MRCPs recorded from T7 (near the left ear), Cz (top of the head), and T8 (near the right ear) can be seen in fig. 4.6.

The study performed an offline evaluation of different types of machine-learning algorithms and features that could be used to detect and classify tongue movements. A linear discriminative analysis (LDA) achieved the overall best performance with an average detection accuracy of 94% for the four movement types and a 63% classification accuracy. The classification accuracy improved further when fewer movement types were used: it increased to 76% for a 3-class BMI with the right, left, and up movements and achieved 88% for a 2-class BMI with the left and right movements.

Thus, the study showed that a decent tongue-movement-based BMI can be achieved, but that while the accuracies were similar to other MRCP studies it was not considered sufficient for a single modality HMI for manually controlling an ARM. Nevertheless, the 3-class BMI was considered very interesting as it could allow an alternative to the SSVEP-based BMI, where left and right attempted tongue movements could allow shuffling between control commands while the up movement could select them. Still, a higher detection and classification accuracy would be needed for manual control of an ARM. It is hoped that long-term usage with the multimodal framework may provide sufficient EEG calibration data to provide a movement-based BMI with sufficient performance. However, within the scope of this thesis, it is concluded that the developed tongue movement-based BMI can only be used in combination with automatic control, where a wrong classification has less impact.

The study is, nevertheless, the first to showcase the great potential of using complex tongue movements. Until now the tongue has only been used as a single class (typically for a four-class classifier in combination with a foot movement, left-hand movement, and right-hand movement. This study indicates that the tongue can be more accurately considered as a "left" and "right" tongue muscle group that can be detected through contralateral MRCPs, similar to left and right-hand movements. The upwards tongue movements are then the activation of both the left and right tongue muscle group, similar to a combined left and right-hand movement. Thus, the 3-class tongue classifier achieves a relatively high accuracy compared to other complex movements (such as finger movements).

Chapter 5. Discussion

5.1 Main findings

This PhD thesis developed and evaluated the first adaptive multimodal control framework for individuals with ALS. It was designed for the transition from using only tongue movements to using only non-invasive brain signals to manually control a 7DoF robot. Tab. 5.1 provides an overview of the developed framework, which can be compared to other single-modality interfaces (Tab 1.1) or multimodal interfaces (Tab. 1.2). While it had already been shown possible to achieve this level of control using tongue movements [27, 28, 31], it was not yet achieved using non-invasive EEG; thus, it was first necessary to develop the methods for allowing manual control of a 7DoF robot using only non-invasive EEG.

Some studies achieved decent control of a robot using spontaneous brain signals [66,67]; however, there is still much work needed before it allows control of a 7DoF robot and requires long training periods and calibrations. For these reasons, it was decided to mainly investigate the use of the much more robust SSVEP control signal for the first versions of the framework. Nonetheless, it was still necessary to develop new SSVEP classification methods.

Most existing state-of-the-art SSVEP classifiers are based on synchronous spelling interfaces with a high information transfer rate, whereby the BMI activates the stimuli for a fixed time period and then classifies which stimulus the participants are focused on. While such classifiers have been used to control robots [45, 46], the control becomes discrete in time (i.e. movements are performed in steps) which is time-consuming and exhausting [45]. During this PhD thesis, three new SSVEP classifiers that perform time-continuous

Table 5.1: The developed interface framework used for ARM control.
✗ : uses modality, ✓: meets requirement, ÷: does not meet requirement.

	Modality					Usability				Control				Robot	Evaluation		
Reference	Lip/Jaw	Tongue	Eye	Evoked Brain	Spontaneous Brain	Modality adaptable	Eyes free operation	≤ 20min calibration	≤ 5 training sessions	Manual	Continuous	Asynchronous	≥ 7 DoF control	Description	ALS	Other	Healthy
This thesis		✗				✓	✓	✓	✓	✓	✓	✓	✓	7DoF ARM and two functional buttons	6	0	10
		✗		✗		✓	✓	✓	✓	✓	✓	✓	✓				
				✗		✓	÷	✓	✓	✓	✓	✓	✓				

and asynchronous classification were therefore developed [155, 161]. Of the three, the recursive spatiotemporal beamformer was selected for the adaptive multimodal framework as it allowed a good performance at a low computational cost.

Study 1 provided the first evaluations of the adaptive multimodal tongue-brain control framework. The experiments with healthy participants showed the advantage of combining tongue- and brain signals if the user can no longer use the full ITCI. It was observed that each subsystem achieved slightly worse performance compared to the prior subsystem (4-34% increase in task completion times), but that all performed significantly faster than the full BMI [166]. The full BMI used much longer time idle in a control mode compared to the other subsystems where the ITCI was used to activate the robot, which highlights the importance of at least one robust and time-continuous control signal. The stepwise decrease in performance observed between each subsystem also shows a possibility to optimize control performance relative to the disease stage, as a 4-34% stepwise decrease in performance is much preferable compared to the 200% decrease in performance there exists between the full ITCI and the full BMI.

Study 1 also evaluated the framework with three individuals with ALS, which highlighted several points wherein the framework needed improvements. One participant had difficulties reaching the distal areas of the MPU but achieved better results on day two. Other studies have similarly shown that the distal areas are the trickiest to activate for healthy participants [169]; thus, it is likely that ALS bulbar symptoms will limit the distal reach of the tongue. Still, the participant was able to properly reach areas on the second day of the trial, indicating that training may improve the tongue's flexibility. All participants noted that BMI stimuli caused fatigue which is a well-known problem for this BMI method, which could be improved by alternative stimulation methods [170, 171]. It was also observed that the framework would benefit greatly by including visual feedback as this could reduce the need to switch visual attention between the robot and the monitor. This was therefore a core building foundation for the framework used in *study 2*.

Study 2 presented an updated framework with several improvements and evaluated it with three participants with ALS [167]. The BMI was improved by increasing the number of electrodes and performing slightly more training per BMI target and the ITCI was improved by implementing a joystick layout [28]. None of the three participants reported the BMI stimuli as fatiguing, which could potentially be caused by the chosen monitor for this study as it had a higher refresh rate (240Hz) compared to the monitor used in study 1 (60Hz). However, it may also be a result of much faster average trial completion times.

All participants preferred one of the hybrid systems, which highlights the importance of a multimodal control framework. While two participants performed well with the tongue control, there first participant performed better with the last hybrid subsystem and the full BMI, despite having reported few bulbar symptoms. With this participant, there was, similar to the first participant of *study 1*, observed issues in reaching the distal areas of the MPU. He also showed improved tongue flexibility on day three, which again could indicate some improved tongue flexibility through the use of the ITCI. While the first participant showed advantages of including BMI signals in the control, the third participant showed the best average performance with each sub-system. Her average task completion times on her third day indicated small decreases in performance between each subsystem (2-21%), while the direct step from the full ITCI to the full BMI caused a performance decrease of 33%. Here, the biggest stepwise increase was between the two hybrid subsystems, which could indicate a need for one more subsystem between the two (similar to subsystem D in *study 1*). While the full ITCI and the full BMI a more similar performance for the third participant in *study 2* compared to the participants in *study 1*, the second participant in *study 2* still highlights the need for a robust control signal. She achieved very similar results as the third participant with the first three subsystems but had very slow times for two of the trials with the full BMI. This indicates that while the full BMI has the potential to achieve similar performance to the full ITCI and hybrid systems, it may not be as reliable as a time-continuous control signal.

Furthermore, the BMIs based on visually evoked potentials are known to achieve drastically worse performance if the user no longer has eye movement [128, 172, 173]. This was one of the reasons that this PhD also investigated the detection of movement intention using EEG. As previously mentioned, studies have shown the possibility of using such signals to gain some control of a robot [66,67,174], but requires a lot of user-dependent calibration data. An idea, therefore, arose: *What if this data could be gathered while the participant used the multimodal framework?*

The pilot studies showed a possibility of detecting and classifying tongue movements using EEG [165] and using the ITCI in combination with EEG to extract the calibration data [164]. However, the detection and classification did not achieve great performance in the pilot study, where an average detection accuracy of 80% was achieved, while the classification accuracy between four movement types was 43%, between three movement types was 55% and between two movement types was 71%. However, it was estimated that to be a viable solution for control a better classifier would be needed. For this reason *study 3* was made.

Study 3 showed great improvements in the detection and classification of tongue movements compared to the previous pilot study [165], by better selection of signal features and classification methods. While the average performance was still lower than necessary, some participants did achieve 100% detection accuracy. It is possible that with more user training and/or calibration data, all participants would achieve this perfect detection accuracy. It also showed relatively good classification accuracies, especially for the 3-class up, left, and right movement classification where an average of 76% accuracy was achieved and for the 2-class left and right movement classification where an average of 88% was achieved. For the two-class classification, it was also observed that some participants achieved 100% accuracy. This performance was higher than that achieved by other studies investigating complex movement types of the hand [175–177]. If a 3-class BMI can be designed with acceptable online performance, it can be utilized to maintain manual control of the 7-DoF ARM using the framework design of *study 2*. Following the interface layout of subsystem TBhCI2 two classes (i.e. left and right tongue movements) can be used to shuffle between control actions, while the last class (i.e. upwards tongue movements) can be used to activate the control action. However, improvements should still be made to achieve this. Studies have shown great success using neural networks that can classify foot, left hand, right hand, and tongue movement with an accuracy of 85% [178, 179], if sufficient data is available. This may also be possible if enough tongue-movement-based EEG should be gathered; it would be possible to gather this data by simply using a hybrid subsystem of the framework over an extended period.

5.2 Limitations

Study 1 and *study 2* included potential end-users for evaluation of the framework, but only three participants were included per study (a total of six different individuals with ALS). While this low number of participants is also seen with other studies involving participants with ALS [44, 180–183], it did provide a limitation for this thesis. ALS is a rare disease but unfortunately often with a fairly rapid progression (with a life expectancy of typically 3-5 years). While there has been good interest in these studies in the Danish community for individuals with ALS, it is difficult to recruit volunteers willing to travel and partake in experiments for long periods of their valuable time. However, the framework has come very close to a state that will allow testing in users' home settings, which would allow a much easier and more rewarding experience for future participants.

The tongue-movement-based BMI from *study 3* has only been evaluated offline with healthy participants. While studies have shown that individuals with ALS can generate movement-based brain signals [164, 180, 181, 183, 184], the proposed BMI should be evaluated online with potential end-users.

5.3 Conclusion

This PhD study developed the first tongue-brain multimodal interface for full control of a 7DoF ARM, based on the idea of an adaptive multimodal control framework for individuals with ALS. The combination of tongue movements and brain signals for control has, throughout the three main studies, been evaluated with 20 healthy participants and six participants with ALS. It has contributed to a better knowledge and insight into the advantages of combining remaining control modalities for both improved performance and as a preparation for the future loss of control modalities. Following the aims and objectives of this thesis, the conclusions are:

A) **Design and development of a framework for a shared tongue-brain control interface:** The developed framework allowed full time-continuous and manual control of a 7.DoF regardless of the selected combination of tongue and brain-based control signals, including the full tongue- and full-brain control.

B) **Implementation and experimental evaluation of the framework:** The evaluation with healthy participants provided a benchmark performance of the framework and showed the possibility of optimizing the performance against remaining tongue functionality.

C) **Clinical evaluation of the updated hybrid framework:** Six individuals with ALS have evaluated a version of the proposed framework. The early evaluations in *study 1* proved that individuals with ALS can utilize the framework to gain control of a 7-DoF arm, but also showed a need for further improvements. *Study 2* showed the benefits of these improvements, including increased visual feedback, joystick control through the ITCI, and an improved BMI. Here, a need for increased BMI control and a desire for a hybrid tongue-brain machine interface was shown, as all three individuals with ALS reported one of the hybrid systems as their favorite subsystem.

D) **Investigation of brain signals generated through tongue movements for a direct tongue-to-brain transition:** *Study 3* showed the possibility of detecting and classifying complex tongue movements using an MRCP-based BMI. It showed decent performance for a 3-class classifier and could possibly be used as a replacement or in combination with the SSVEP-based BMI used in the framework if the user no longer can or wishes to use SSVEP-based control. However, improvements to the MRCP-based BMI would still be required or a great loss of performance would be expected.

5.4 Future perspectives

To gain much better evaluations, the framework should be tested for long-term use in the user's home settings. This will allow a further evaluation of the systems training effect and the progression between subsystems. Furthermore, it will be tested in more realistic situations than those arranged in experimental trials. It will also allow long-term recordings of tongue movement-based brain signals, that could be used for an improved tongue movement-based BMI.

For home-use evaluation, it may also be beneficial to investigate other control modalities. While this thesis focused on a tongue-brain framework, the core idea of an adaptive human-machine interface framework should not be limited to only these technologies. Every individual is unique and so is the progression of ALS symptoms. An adaptive human-machine framework should therefore allow the inclusion of any remaining control modality (EMG, Eye-tracking, finger movement, etc.), to further improve the tailoring of a system to the individual.

Still, both an ITCI and a BMI have advantages and should always be considered a valuable asset to a multimodal framework. The ITCI provides excellent control with little training and no requirements for calibration. Furthermore, it is intraoral and thus not visible while used, which gives it an aesthetic advantage over many other control modalities. However, the ITCI used in this PhD study does require a tongue piercing which not everyone will accept [162]. However, recent studies have investigated a new piercing-free ITCI which should be considered for future frameworks [100].

Similarly, the use of a more aesthetic EEG headset should also be investigated, such as in-Ear EEG [185, 186] which could also prove very beneficial for tongue movement detection (since the tongues are represented near the ear on the motor cortex). Alternatively, as SSVEP is measured from the back of the head it may be possible to integrate an EEG headset into the headrest of the user's wheelchair.

Lastly, while the framework evaluated in this thesis provides manual control, as this is considered an essential component in any end-solution, the implementation of automation will certainly improve the performance and should therefore be considered as an optional integration. Ideally, it should be implemented in such a way that allows the user to select the level of automatic assistance, as automation may impact their feeling of independence.

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