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A Translational Roadmap for a Brain-Machine-Interface (BMI) System for Rehabilitation*

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***Abstract*—In this communication, a translational roadmap for a noninvasive Brain Machine Interface (BMI) system for rehabilitation is presented. This multi-faceted project addresses important engineering, clinical, end user and regulatory challenges. The goal is to improve the feasibility of at-home neurorehabilitation for patients with chronic stroke by providing a low-cost, portable, form fitting, reliable, and easy-to-use system. The proposed BMI system is also designed to enable direct communication between the end-user and clinician, allowing for continuous patient-specific rehabilitation optimization.**

I. Introduction

There are about 7.2 M persons living with stroke [1]. Stroke is the primary cause of long-term disability in the US, leading to reduced quality of life and social stigma, with many of them requiring long-term care. With more than ~800,000 people having stroke in the US every year, and a global market size expected to reach $31B by 2021 [2], there is a pressing need for novel stroke rehabilitation tools and devices for in-clinic and at-home use for sustainable long-term therapy that also promotes cortical reorganization toward recovery. Unfortunately, simple rehabilitation tools (passive exercisers) and more sophisticated devices (such as robot-assisted therapy devices) fail to engage and motivate the patients, are hard to match to their needs, or are limited to clinical settings. Moreover, these systems do not necessarily promote motor relearning towards recovery, are costly and/or difficult to deploy for in-home use. To promote motor reorganization, developers are now turning to devices equipped with interfaces for video gaming and virtual reality, but these technologies are still in the very early stage of development. Thus, there is a lack of safe, effective, engaging, and low-cost smart neuro-rehabilitative systems that can provide clinic and home-based sustained long-term neuro-recovery of motor function for stroke survivors.

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Current stroke rehabilitation roadmaps are adapted from the clinical practice guideline endorsed by The Stroke Council of the American Heart Association [3]. Based on stroke severity, the healthcare professional decides on inpatient/outpatient interventions. Inpatient rehabilitation starts with the assessment of the type and intensity of the rehabilitation. The clinician monitors the patient's recovery and decides if there is sufficient improvement for the patient to live in the community again. If not, the rehabilitation continues at the clinic, the extent of which depends on patient status and insurance benefits. If there is sufficient improvement, the patient can get discharged. At this point, the process merges with the outpatient rehabilitation practices. If necessary, a suitable rehabilitation practice starts or continues as outpatient. If not, the patient is left with an option to continue home-based exercise routines. Home rehabilitation process can vary greatly as at this point the clinician's involvement is minimal, and feedback is provided on the basis of clinical follow-ups, if any. On the other hand, if the rehabilitation continues as outpatient, the clinician checks if optimal recovery is reached or the recovery is plateaued, resulting again in often self-applied home exercise routines (if the patient is motivated and/or there is family support) and clinical follow-ups.

Whether the rehabilitation occurs at the clinic or at home, the main issues that are often faced by the patients are: 1) the limited duration of the therapy routines, 2) the cost and accessibility of the inpatient/outpatient therapy and devices, and 3) the lack of established norms for home exercise routines/therapy. The main challenges for the healthcare professional are: 1) monitoring and tracking the patient's progress, 2) lack of reliable metrics (currently based mostly on observation), and 3) engaging the patient thereby promoting cortical plasticity, which perhaps is the most critical component on stroke rehabilitation [3]–[6]. Importantly, there is currently no established framework that combines the therapeutic roadmap to provide sustained long-term therapy for individuals with stroke at home, with medical devices that a) can continuously monitor/log patient status for clinicians, b) provide human-centric assessment metrics to assess success of the intervention, and c) promote patient's engagement to the therapeutic session in an effective way.

To address these unmet needs, we are engineering a system with diagnostic, assistive and therapeutic functions that is safe, cost-effective, and reliable, with advanced form factors, connectivity for clinician monitoring, and embedded high performance processing capabilities that users want to wear and benefit for extended periods of

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time. In this paper, we review our translational roadmap for the proposed neurorehabilitative system for stroke rehabilitation.

II. Methods

The design of the Brain-Machine Interface (BMI) system is based on our patented decoding and signal denoising algorithms for real-time BMI applications [13], [24], [27], [28]. Specifically, we have demonstrated the feasibility of inferring gait kinematics and surface electromyography (EMG) patterns, as well as non-locomotive (e.g., sit-to-stand) movements from active-electrode scalp electroencephalography (EEG)[7]–[11]; we have developed real-time adaptive noise cancelling algorithms for identifying and removing artefactual components from scalp EEG that increase the signal to noise ratio [12], [13], [24]; multi-day, real-time, closed-loop EEG-decoding of the lower-limb kinematics [14]–[16]; and adaptation to visual-motor gait perturbations during real-time closed-loop BMI control of a virtual avatar suggesting that BMIs can be used to promote cortical plasticity [14]–[16].

The translational research and development of the BMI system, supported under a National Science Foundation Partnerships for Innovation (PFI) award, is comprised of three main components: 1) the BMI Module, 2) the Information and Control (IC) Module, and 3) a multifunctional single degree of freedom Upper Limb Rehabilitation Robot as the initial robotic platform. A schematic of this system is presented in Figure 1.While the system is shown as being operated with the actuator at the elbow, the BMI system is not limited to this setup and is also intended to be applicable for a variety of upper limb rehabilitation methods programs.

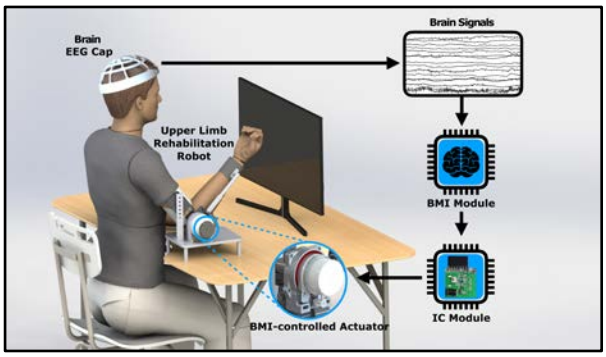

Figure 1: BMI system diagram, which highlights the three major components: the BMI module, the IC module, and the upper limb rehabilitation robot.

A. Brain Machine Interface (BMI) Module

BMI systems seek to translate neural brain patterns to machine-acceptable commands using mathematical mapping tools called decoders, which infer the user's motor intent. Depending on the interfaced systems and intended applications, these mapping tools can be formulated in the form of continuous-profile model-based decoders to interpret time varying parameters of action from neural signals (i.e., leg/arm joint angles, joint velocities, surface electromyographic (EMG) patterns) using Kalman or Weiner filters [7]–[11], [16], or in the form of neural classifiers that map discrete states of neural patterns to discrete classes to be controlled (e.g., stand-up, turn left or right, stop, etc.) [13], [17]. Given the spectrum and extent of motor deficits observed in clinical populations, BMI-robot systems require some form of shared control/shared autonomy. In our shared-control classifier application, we have shown that multiple classes of user intent can be decoded via non-invasive EEG measurements. With our exoskeleton-BMI system (NeuroRex), we have applied our neural classification methodology for the control of a robotic lower-limb exoskeleton (REX, REX Bionics Inc.) [26] for persons with paraplegia [15]-[16].

B. Information and Control (IC) Module

The information and control module is the gateway of the BMI module to the rehabilitation hardware. This module provides input/output capability with high data transfer rates, featuring two major functions: driving the rehabilitation device's actuators according to the output of the BMI module (decoded neural intent) and sensory data logging, transmission and feedback to the BMI module for generating smart metrics regarding the rehabilitation and tracking patients' functional improvements and logging them for the clinician's review. This unit will also provide a view screen to supply visual feedback to the patient on his/her performance for the given tasks in addition to the kinesthetic feedback supplied by the usage of rehabilitation hardware. The interface will also be used to provide patient and rehabilitation session data, necessary logs and metrics, as well as tools for comparative analysis among subjects and rehabilitation sessions [19]. As new subject and new rehabilitation sessions are registered, this logging interface will form an invaluable database for engineers, clinicians, neuroscientists, physiotherapists and other researchers. There is currently no test bed that is used for rehabilitation that can provide multimodal data to form a database, across sessions and patients.

C. The Single Degree of Freedom Upper Limb Rehabilitation Robot

As a proof-of-principle device, we propose to focus on upper extremity rehabilitation with the use of a single degree of freedom upper limb rehabilitation robot. The system is interchangeable in that the BCI module will be able to control any robotic system, given the system's specific I/O protocol is provided. With the current device, the patient will be in a seated position (on a chair/wheelchair) holding a single handle. This will allow us to focus on unilateral synchronized rehabilitation. The handle will be sensorized to allow us to measure the torque/load applied by the patient's arm. The overall

actuated system will allow us to use the following modes of operations; fully assistive: the system moves the arm for the patient once the intent is detected; assist as needed: the user provides some level of control, the remaining assistance to reach the target force, position or velocity (clinician prescribed tasks) will be provided by the system once the intent is detected, and; resistive: the patient is able to apply full input necessary to reach the goal, however, the system applies adjustable levels of resistance to his/her motion to improve gradually the muscle activation levels, once the intent is detected.

III. Technical Challenges

The rationale of choosing the above described main components and the overall development strategy is closely related to the major technical challenges identified towards the meaningful commercialization and wide-scale deployment effort of the proposed BMI module (depicted in Figure 2).To our knowledge, there is no available FDA-approved smart neurorehabilitation system in the market. The following sections will describe the challenges and will present strategies in how to handle each challenge.

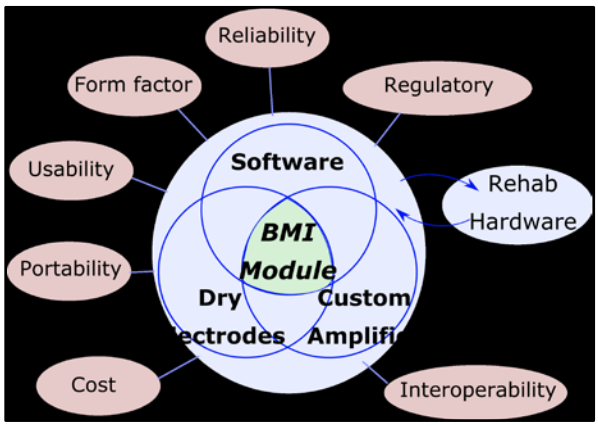

Figure 2: Technical challenges to commercialization (red)

A. Cost

Current high quality EEG recording systems, including their amplifiers and software, are designed as general purpose systems mostly for research purposes. The cost of such systems are naturally very high (>$25K), preventing them as good fits for commercial BMI modules. These systems also have closed/proprietary architectures making their integration to custom, small form factor hardware increasingly difficult. Therefore, the design of low-cost and small form factor EEG amplifiers with high inter-operability with external robotic-guided rehabilitative systems is crucial for both commercial and academic research applications. This could be in the form of a daughterboard, attached to a credit card sized System of Module (SOM) module. SOM's are a type of embedded computer system that would replace the large amount of computer hardware typically necessary for real-time processing of EEG signals. Additionally, an example SOM, such as the National Instrument's Field Programmable Gate Array (FPGA) supported high-performance SOM, which can cost under $1000, which helps to reduce the overall cost. For EEG sensors, commercial dry EEG electrodes should be used, considering the high development effort and development cost of such components. Current dry EEG sensor technology can easily be interfaced to our custom amplifier hardware with no additional development or modification needed. It is also important to minimize channel count, in favor of a low-cost personalized architecture. As compared to gel-based wet electrodes, dry electrodes are typically thought to collect EEG with a lower signal quality and susceptible to artifacts. However, recent research on complex naturalistic settings with freely-behaving individuals suggests the feasibility of obtaining high signal quality can be achieved with dry electrodes as compared to the wet electrode alternatives [20], [21], [24].

B. Portability

The portable nature of any proposed system is vital for large-scale deployment for home use, which greatly expands the feasibility of home-based data collection, diagnostics and therapeutics. Current EEG measurement systems and most robotic rehabilitation devices are large and costly. Thus, successful BMI-robotics systems must be both portable and low-cost to increase the likelihood of adoption by end-users.

C. Interoperability and Usability

Two identified challenges in the translation of clinical BMI systems are lack of interoperability and poor usability in the field [25]. The BMI module's input/output structure must be designed to be interoperable (i.e., 'plug in') to any suitable physical or virtual robotic rehabilitative system. Our proposed active upper limb rehabilitation machine I/O layer will lay the groundwork for assessment of interoperability of our system by other active devices. Although the single degree of freedom robotic device is focused on the upper-limb, it should be noted that it can be modified for upper or lower body interoperability and therefore has broad applications for similarly defined BMI research in clinical and non-clinical areas.

System set-up represents an important usability challenge as in current noninvasive BMI systems, the EEG electrode density and electrode cap set-up require long preparation times and can lead to user errors in cap placement or signal integrity due to high electrode impedance or electrode pop-up [21]. Our group has made significant progress on optimizing the most relevant electrode spatial locations by choosing the most information-rich channels for decoding, for both able-bodied, and individuals with spinal cord injury (SCI) [18] and stroke [22]. This not only reduces the number of channels, but also leads to the availability of selective channel locations, per subject, depending on their clinical condition. We expect that with personalized headsets, reduced channel count and the use of dry electrodes will lead to reliable quick setup-to-recording time of less than 2 minutes, without requiring expert input.

D. Form factor

The use of feedback from focus groups on the form of the EEG sensor headset/cap for reliable and long-term usage can help to address the technical challenge of form factor that also affects usability. The selection or design of the EEG sensor cap is an iterative process that will likely lead to several form factors to accommodate the needs and desires of the end-users for wide-scale deployment.3D handheld scanners and 3D printed prototyping in collaboration with design professionals now allow for the design and manufacture of customized electrode holders and headsets that could be combined with other wearables such as headphones, as an alternative to traditional soft/meshed caps or the newer semi- or rigid EEG helmets that can be found in the consumer electronics market. We have done an extensive comparative effort of the form factor and usability of different commercial EEG systems [21] that adds to the knowledge base of the long-term usability of different designs.

E. Reliability

Planned wide-scale deployment of such a system at the clinic or at home requires reliable mechanical components and electronics systems, especially considering the unattended home use. It is important for commercial BMI applications to follow accepted standards in compliance with the regulatory norms (e.g. FDA and National Institute of Standards and Technology –NIST- traceable norms).It should be noted that the creation and adoption of standards for BMI systems is one of current challenges in the field [25]. Further regulatory challenges are discussed in section IV.

F. Denoising algorithms

A technical challenge in EEG-based BMI systems is the presence of physiological and non-physiological artifacts that are superimposed onto the neural signals measured from the scalp recording areas. Ocular artifacts, for example, are present in most EEG recordings, and, due to volume conduction, corrupt measurements from all electrode locations in changing profiles and amplitude distributions. Artifacts are perhaps one of the major factors challenging the high accuracy real-time applications of these systems. Our laboratory has developed a generalized real-time de-noising framework for high performance artifact cleaning based on the robust adaptive H^{∞} filtering formulation [13] [24]. We have shown the effectiveness of our technique for cleaning eye-blinks, eye-movements, signal bias and signal drifts, for60 EEG locations simultaneously, in real-time [13], and more recently, motion artifacts [24]. One important advantage of our method is that it depends on the real-time measurement of the noise source. This might seem like a disadvantage at first due to its requirement of additional sensory measurements, however, compared to other existing methods that depend on the definition of clean EEG segments, or estimated statistical distributions, it allows us to be very selective on what is removed from the EEG measurements. Having this capability allows us also to identify the possibly time-varying artifactual components and recover in real-time the actual EEG data that is contaminated by the artifacts. In [13] and [24], we have established a scientific premise regarding the motion-related artifacts and their adverse effects on EEG signal processing. It should be noted that the proposed initial BMI rehabilitation system is designed to accept the patient in a seated position, thus minimizing the presence of motion artifacts. Nevertheless, our group has analyzed the effects or presence of motion artifacts in treadmill walking [12] [24] and found that even in normal walking speeds, the motion artifacts were found to be negligible to non-detectable.

IV. Commercialization Strategy

A well-defined commercialization strategy will significantly increase the ability to overcome the many regulatory and commercial challenges in the path towards commercialization. Approaches to addressing the regulatory and commercial challenges were developed through close collaboration with clinicians, patients, and business leaders during the Commercializing Innovation (C3i) program [22]. Figure 3 presents the 3-phase commercialization strategy with each phase lasting approximately one year.

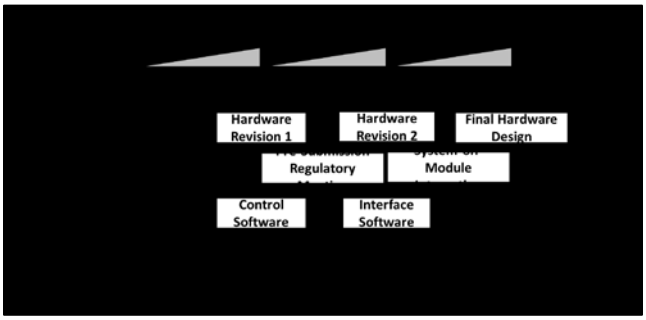

Figure 3: Commercialization pipeline with intended hardware, software, and regulatory milestones highlighted. This assumes that intellectual property (IP) has been adequately protected.

A. Regulatory Challenges

Regulatory approval is one of the challenges that must be carefully navigated for timely and cost-effective commercialization of the proposed system. To accelerate technology transfer, it is imperative to work closely with regulatory agencies (e.g., US Food and Drug Administration or FDA), and make use of their pre-submission program, and/or new pathways for innovative devices. Proof-of-principle data acquired during early feasibility trials could serve as data for regulatory purposes. Thus, experimental design and outcome variables should be discussed with the FDA to ensure it meets their regulatory requirements.

B. Validation of the Customer Needs and Business Model

Our initial business plan (one must remain flexible to adapt to changing conditions) has been shaped by three key components that include 1) our team's experience with the Concept to Clinic: Commercializing Innovation (C3i) Program[22], 2) a core set of industry experts in rehabilitation robotics and embedded/instrumentation

systems with experience in the NSF I-Corps program, and 3) the benefit of an established business model in the market segment of rehabilitation robotics for inpatient rehabilitation facilities. The NSF I-Corps program helps to prepare scientists who are in the process of moving basic-research projects towards commercialization, while the C3i program is an industry-recognized approach towards biomedical research translation. Experience and participation with the these two programs, and with the assistance of the University of Houston's Office of Tech Transfer and Innovation, helps to validate the business hypotheses regarding commercialization of advanced rehabilitation robotics by interviewing potential customers and to validate the market opportunity and minimize unexpected risk with the mentorship by program instructors and successful entrepreneurs within the industry. Additionally, focus group feedback to our proposed system by physicians, physical therapists, and patients began early in the project and will continue to be a key factor in maintaining patient-oriented designs and maximizing usability.

C. Optimizing Key Roles and Metrics

During the multi-year effort towards a proof-of-principle device development, and beyond, key personnel roles will be optimized in accordance with the defined metrics, at multiple levels. One of the 1st order project metrics can be defined as the pre-defined milestones and year-end deliverables. Since the deliverables of a commercial BMI module targets multiple users, the throughput of per year-end deliverables may be used as an additional metric. Proof-of-principle device performance on BMI decoder accuracy, subject task completion accuracy and time, overall setup-to-usage time of the device at each level of development, from all subjects, can be logged and used as improvement points for the next iteration. Software efficiency metric can be calculated as, for example, errors/bugs per 1000 lines of code, and adjustments can then be made accordingly. As the proposal nears the mid-term of the multi-year timeline, 2nd order metrics can be employed, such as; device delivery to subjects (scheduling time and cost), loss of system availability and cost due to maintenance and repairs, estimated cost of delivery delays and its reasons, and overall project cost for projected future deliveries. Finally, in the final stages of the timeline, 3rd order metrics can be used to help define the future production costs and improvement points, overall weight and form factor of the final proof-of-principle device, and measure mean time between failures/errors, to gauge the efficiency of the device. Additional metrics that spans the full duration of the proposal may include: Number of customer needs identified (to gauge the effort in identifying the future need), number of in-process changes (gauging the overall plan effectiveness), assembly efficiency (gauging the design -mechanical and electrical-efficiency), percent of sub-milestone dates met (gauging the team efficiency), and percent of parts used in multiple products (to gauge the parts' generality/effectivity towards reducing the future costs). The measured cost, development effort and effectiveness metrics can then be used towards iterating our design to a Minimum Viable Product (MVP).

D. Envisioned Plan beyond the Project

The deliverables of this commercialization strategy are 1) the definition of specific gain creators and pain relievers that are based on in-person customer/prospect interviews and feedback obtained after demonstrations using a minimum viable product (MVP), 2) a definition of specific value propositions (VPs), cost structure and revenue streams that will help to create a path to successful commercialization of the proposed smart co-robot system, and 3) submission to FDA for regulatory review and approval.

V. Conclusion

The high-cost and expertise required for current state-of-the-art rehabilitation systems is prohibitive for most chronic stroke survivors seeking rehabilitation. Therefore, there is a need for reliable neurotechnologies that engage the user, are low-cost, and can be deployed at home. The commercial and societal impact potential for the proposed BMI-based stroke neurorehabilitation is two-fold:

Innovation ecosystem: An integrated user-centered research-driven translational roadmap for accelerating innovation, translation, and entrepreneurship of BMI systems for therapeutics and diagnostics has been presented in this paper. The proposed BMI system will benefit students, faculty, industry, and end users. Engagement of end users and regulatory agencies early in the design process is expected to ensure the system is responsive to the needs of the end users and complies with regulatory guidelines for safety and efficacy. This should ensure faster translation of the system to the end users.

National Impact: The US market for a smart therapeutic system for rehabilitation after stroke is estimated to be $1.2B. Moreover, smart neurotechnologies that safely and quickly interface non-invasively with the nervous and the body represent a major opportunity for innovation in the US industry over the next decade. A commercial BMI system will also accelerate scientific discovery in human and clinical neuroscience; significantly improve national health; boost innovation in wearable therapeutic neurotechnologies, and empower individuals to gain awareness and take control of their own healthcare and wellness.

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