1. Publishable summary

This section should be of suitable quality to enable direct publication by the Commission. Please ensure that it is set out and formatted so that it can be printed as a stand-alone paper document not exceeding four pages. It shall also reflect the website of the project (if applicable).

Please include a summary description of the project objectives, a description of the work performed since the beginning of the project, a description of the main results achieved so far, the expected final results and their potential impact and use (including the socio-economic impact and the wider societal implications of the project so far). You should update this publishable summary at the end of each reporting period.

Please include also, as appropriate, diagrams or photographs illustrating and promoting the work of the project, the project logo and relevant contact details.

The address of the project public website should also be indicated, if applicable.

1.1 Summary description of project objectives

Tremor is the most common movement disorder and it is strongly increasing in incidence and prevalence with ageing. More than 65% of the population with upper limb tremor presents serious difficulties in performing activities of daily living (ADL). Tremor is not life-threatening, but it can be responsible for functional disability and social inconvenience. It is typically managed by means of drugs, surgery (thalamotomy), and deep brain stimulation, but treatments are not effective in approximately 25% of patients.

The main objective of the project is to validate, technically, functionally and clinically, the concept of mechanically suppressing tremor through selective Functional Electrical Stimulation (FES) based on a (Brain-to-Computer Interaction) BCI-driven detection of involuntary (tremor) motor activity:

- The system will detect and monitor involuntary motor activity (tremor) through a multimodal BCI. The proposed BCI will combine CNS (Electroencephalography, EEG) and PNS (Electromyography, EMG) data with biomechanical data (Inertial Measurement Units, IMUs) in a sensor fusion approach. It will model and track tremor and voluntary motion.
- It will also include a multi-channel array FES system for selective stimulation of muscles for tremor suppression while reducing the influence on voluntary motion.
- For a potential commercial exploitation the embodiment must fit potential user expectations in terms of cosmetics, functionality and aesthetics.

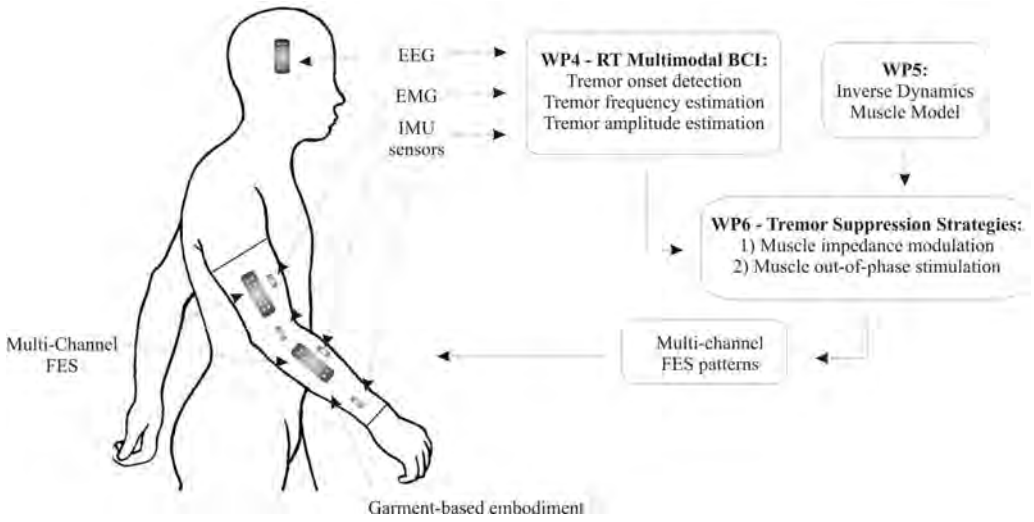

Figure 1. The TREMOR concept: (1) a multimodal BCI system integrates information on brain activity, muscle activity and limb movement for a robust detection of tremor parameters (onset, amplitude and frequency), (2) an inverse dynamics muscle model provides information on required muscle activation parameters to attain (a) muscle impedance modulation and (b) muscle out-of-phase stimulation, (3) a multichannel FES system closes the human-in-the-loop system within fatigue and pain limits.

TREMOR proposes a multimodal BCI in which the main goal is identifying, characterizing and tracking involuntary motor bioelectrical and biomechanical activity as a command to trigger a biomechanical suppression of tremor. The concept of TREMOR is graphically depicted in figure 1.

The TREMOR consortium set up a methodological approach and a work plan to attain project's objectives. This work plan consisted of nine (9) work packages, of which the ones active during this reporting period are briefly described in the following paragraphs:

WP1: Elicitation of User Needs & Neurophysiological study was coordinated by Université Libre de Bruxelles (ULB, Partner 4) and led by Prof. M. Manto. The objectives for this reporting period were the updated analysis of the state-of-the-art.

WP4: Multimodal BCI for tremor identification, characterization and tracking was coordinated by Consejo Superior de Investigaciones Científicas (CSIC) and led by Prof. J.L. Pons. The objectives of this WP are during this period were: (1) to assess the performance and computational complexity of different sequential compound signal separation techniques suitable for real-time extraction or/and enhancement of component corresponding to tremor from reduced set of EEG channels; (2) to implement and validate self-adaptive tremor detection from EEG; and (3) to characterize and quantify tremor in neural drive to muscles. These thre objectives correspond to the additional tasks included during the second amendment to the project (inclusion of UM in the framework of TREMOR-EEU).

WP6: Control strategies for FES active & semi-active tremor suppression was coordinated by CSIC and led by Prof. J.L. Pons. The aims of this WP for this period were related to the recommendation from the previous review process on the need to update deliverable D6.1.

WP7: System integration was coordinated by Technaid (partner 8) and led by Mr. J. Roa. The objectives of this WP were: (1) To integrate all the system components and (2) to technically support experimentation in WP8.

WP8: Functional and clinical validation. Usability analysis was coordinated by ULB and led by Prof. M. Manto. The objective of this WP is to prove the concept of FES suppression of tremor and the analysis of case studies.

WP9: Exploitation and dissemination was coordinated by Technaid and led by Mr. J. Roa. The objectives of this WP were: (1) To investigate the possibilities for commercialization of TREMOR outcomes; (2) To investigate commercialization of sub-outcomes of TREMOR; (3) Protection of exploitable results; and (4) Dissemination of scientific results.

1.2 Results in the reporting period

WP4

Within WP4 the deliverables "D4.2 Algorithms for tremor extraction and onset detection from EEG" and "D4.3 Motor unit characteristics during tremor" have been submitted in due time. They collect methods, materials, results and discussions following activities WP4.6, WP4.7 and WP4.8.

WP6

In the framework of this WP, an updated version of deliverable D6.1 has been issues as a consequence of the recommendations from the previous review process.

WP7

Within WP7, the deliverable "D7.2 Integration of EEG detection with a tremor suppression system" has been submitted with slight delay due to a slightly longer quality check on the document and the originally not planned integration of two different prototypes.

WP8

In the context of this WO all necessary experimental trials with tremor patients have been performed to reach a proof of concept and to analyse case studies. All these results have been collected in deliverable D8.2.

WP9

In this WP, a detailed dissemination and use plan together with detailed exploitation plans for the exploitable results of the project. The dissemination and use plan is included in deliverable D9.2 whereas the business plans are included in deliverable D9.3.

2. Project objectives for the period

Please provide an overview of the project objectives for the reporting period in question, as included in Annex I of the Grant Agreement. These objectives are required so that this report is a stand-alone document.

Please include a summary of the recommendations from the previous reviews (if any) and indicate how these have been taken into account.

According to Annex I to the TREMOR contract, the milestones set for this period (month 29 through month 36) are (please refer to Table 2 for more details on milestones):

- M4.6, Algorithms to extract tremor component from EEG defined
- M4.7, Algorithms to detect tremor onset from EEG defined
- M4.8, Individual motor unit characteristics during tremor identified
- M7.4, Active garment for tremor suppression delivered
- M7.5, Overall system integration
- M-II, Functional active garment for FES tremor suppression via a BCI identification of tremorous motion.
- M9, Evaluation of the TREMOR and associated concepts with regards to commercial interests
- M-III, Functional, clinical and usability evidence of the TREMOR concept
- M-IV, Evaluation of the TREMOR and associated concepts with regards to commercial interests

In addition to these milestones, two milestones from the previous period were only partially approved during the review (as per the consolidated Technical Review Document, Ref. Ares(2011)434003):

- M2.2, Product requirements document delivered
- M3.3.B, Functional multi-channel EEG, EMG, IMU and FES system delivered

All these milestones are now considered met following the delivery in due time of the following project deliverables:

- D1.3, Updated review of the SoA (three updates). Two issues of this document have been submitted. The first one corresponds to the resubmission of the updated analysis of the SoA submitted for review during the previous period according to the recommendations in the consolidated Technical Review Document for the second project review. The second delivery updated the previous one up to the end of the project and compares project studies and results to those found in the literature.
- D4.2, Algorithms for tremor extraction and onset detection from EEG
- D4.3, Motor unit characteristics during tremor
- D7.2, Integration of EEG detection with a tremor suppression system
- D8.2, Case studies and analysis of functional, clinical and usability evidence of TREMOR system
- D9.2, Dissemination and Use Plan (DUP) for TREMOR
- D9.3, Preliminary business plan for exploitable results
- D10.1, Demonstration material
- D11.4, Report on networking activities

During this period we have implemented a number of reactions to the recommendations included in the last review Technical Review Document:

R1: Owing to the gap between deliverables submission and periodic reviews, important information on progress detailed in the periodic report is not reflected sufficiently in the corresponding deliverable reports. The consortium is advised to include an up-to-date summary of new progress as an annex to relevant

deliverables. Also, it is recommended that the next periodic report focuses on the achievements of the period under evaluation.

> Action R1: This is not applicable to most of the deliverables in this period due to the short duration (month 29-month 36). However, it has been included in Deliverables D4.2 and D4.3, which are the "eldest" with respect to the preparation of this Periodic Activity Report.

R2: Resubmitted deliverable reports should include a document change history record, so that amendments easily can be identified and compared with earlier versions.

> Action R2: Done, this document change history record has now been included in D1.3 and D6.1.

R3: State of the art update activity should be more methodological. A bibliography of significant papers published outside the consortium should be maintained and updated regularly.

> Action R3: This has been taken into account for the preparation of the resubmission of D1.3 (month 24) and the new update of this document (month 36).

R4: Pain and fatigue assessment has started on a group of five patients. Preliminary results indicate that the device is well accepted by patients. It is important to validate these results by a systematic analysis on more patients.

> Action R4: Additional assessments on fatigue and pain have been developed during the validation of the final platform in the framework of WP8.3 and they are reported in deliverable D8.2. Results indicated that the strategies are acceptable by users and the strategies developed do not induce fatigue.

R5: At this stage, FES is not yet operative through electrode arrays (only individual electrodes are used), thus limiting the efficiency of the device. It is recommended that this issue be solved rapidly in order to leave sufficient time for full integration.

> Action R5: The consortium decided to split the validation of FES through electrode arrays in two steps, namely, the validation of muscle selectivity and the validation of tremor suppression. These validation steps were implemented in the framework of WP8.3 and are reported in D8.2. On the one hand, the consortium developed novel algorithms to calibrate the electrodes arrays over the forearm of humans and improve selectivity. These novel algorithms allow the rapid calibration of the matrix (based on twitches) on human arm with a high selectivity (avoiding movement of the fingers). On the other hand, results demonstrated the efficacy of the FES-based tremor suppression strategies. These experiments were based on single electrodes mainly: 1) To reduce the duration of the experimentation with patients, 2) Due to the fact that the second prototype based on textiles presented some limitations for the trials with patients (see deliverable D8.2), 3) the impact of the matrix in the validation of the strategies is minimal.

R6: The BCI prediction of voluntary movement has led to promising experimental results in the lab environment. However, precision and recall drastically change from one patient to another. The consortium is advised to investigate on which class of patients the method works best.

> Action R6: The experimental trials show that there is no correlation between pathology and performance of the algorithms for BCI prediction of voluntary motion. This finding is consistent with previous results in the literature that show that ERD/ERS is not present in all subjects. Despite the low number of samples for each group, only a significant difference between the power decrease of the patient groups above and below 65 years old was found ($F=8.686$, $p=0.016$, $\alpha = 0.05$). Nonetheless, these results were expected a priori since the influence of the age on the sensorimotor rhythms is well documented in the literature.

R7: Stakeholder outreach could be improved, especially in co-opting direct involvement of MS, ALS, and Parkinson's associations (national and international).

> Action R7: During the validation of the final platform the TREMOR consortium got in contact with different association from different pathologies. In particular, Asociación de Parkinson de Valencia collaborated actively in the validation phase of the project. In addition, CSIC got in contact with several hospitals in Spain in order to validate the application of such device in tremor due to Multiple

Sclerosis (MS). The contact person was Dr. Julián Benito-León (neurologist of Hospital 12 de Octubre - Spain - and president of Spanish MS patients association). A protocol for the trials was drafted and submitted for Ethical Committee approval. The consortium is currently waiting the approval to proceed with the studies with other pathologies. Other hospitals were contacted and expressed their intention to collaborate in future studies, such as Hospital de Getafe (Dr. Lorenzo Morlán, Spain) and Columbia University School of Public Health (Prof. Elan Louis, Dr. Pullman).

R8: The consortium is required to provide a suitable business plan draft by the next review, in order to achieve an even more concrete approach to a real exploitation scenario.

Action R8: This is included in deliverable D9.3.

R9: Minimum necessary resources should be applied for non-essential dissemination activities (especially travel and conference attendance).

Action R9: This has been reduced to a minimum, still very relevant conferences (e.g. IEEE EMBC 2011) have been attended.