Gait Analysis and Quantitative Drug Effect Evaluation in Parkinson Disease by Jointly EEG-EMG Monitoring

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Astract –This work addresses the rising need for a diagnostic tool for the evaluation of the effectiveness of a drug treatment in Parkinson disease, allowing the physician to monitor of the patient gait at home and to shape the treatment on the individual peculiarity. In aim, we present a cyber-physical system for real-time processing EEG and EMG signals. The wearable and wireless system extracts the following indexes: (i) typical activation and deactivation timing of single muscles and the duty cycle in a single step (ii) typical and maximum co-contractions, as well as number of co-contraction/s. The indexes are validated by using Movement Related Potentials (MRPs). The signal processing stage is implemented on Altera Cyclone V FPGA.

In the paper, we show in vivo measurements by comparing responses before and after the drug (Levodopa) treatment. The system quantifies the effect of the Levodopa treatment detecting: (i) a 17% reduction in typical agonist-antagonist co-contractions time (ii) 23.6% decrease in the maximum co-contraction time (iii) 33% decrease in number of critical co-contraction. Brain implications shows a mean reduction of 5% on the evaluated potentials.

Keywords—EEG, EMG, MRPs, Gait, FPGA, Parkinson desease, Levodopa administration

I. INTRODUCTION

Parkinson's disease (PD) is a long-term degenerative disorder of the central nervous system, resulting in motor impairment. Typically, the cardinal features of PD are resting tremor, rigidity, bradykinesia and gait disturbance followed by disequilibrium [1]. Nowadays, PD affects 1% of the over 60 year-old population and the 4% of those over 80: globally, about 7 million people [2]. In Parkinson's disease, certain nerve cells (neurons) in the brain gradually break down or die. Many of the symptoms are due to a loss of neurons that produce a chemical messenger in the brain called dopamine. When dopamine levels decrease, it causes abnormal brain activity, leading to signs of Parkinson's disease.

In order to make personalized medicine be successful, the major challenges to address are the development of accurate diagnostic tests that detect a pathology in its early stage and identify patients who can benefit from targeted therapies. Emerging new tools in PD analysis such as molecular imaging (PET/SPECT imaging) [4] and OMICS [5] have made it possible to customize the health care of individual PD patients, basing on a physiological and pathological knowledge of the subtype and the stage of the disease [3]. The Deep Brain Stimulation (DBS) is a promising surgical procedure for the treatment of advanced PD. The mechanism of DBS [6] is blocking abnormal neural signals, which lead to clinical symptoms of PD sending electrical impulses to specific brain regions. From the perspective of precision medicine, one of the key considerations in DBS is selecting the most effective target area individually for the specific patient. These types of prognostic approaches are highly accurate, but they still do not allow a real-time evaluation of the impact. Furthermore, DBS is an invasive technique suggested only in advanced PD patients due to the high cost of the operation and because of the need of change the implanted device every 10 years.

Instead, on the drug side, no significant progress has been achieved: the Levodopa, releasing dopamina, has remained the most effective treatment since 1960. Nevertheless, the scientific community has demonstrated a very high variability of the efficacy of a single treatment from one subject to the other [3]. Some patients also develop severe side effects that make, de facto, their situation even worse.

In the meantime, wearable sensor technology offers an encouraging solution to the above-mentioned challenge since it performs high degree of objectivity, sensitivity, good accuracy and real-time operability, allowing the monitoring during the everyday life with a discrete comfort degree. Interesting wearable solutions have been proposed in literature aiming help patients with therapeutic administration, by using automatic assessment of gait analysis indexes. eGaIT system [7] and Parkinson's Kinetigraph based (PKG) system [8] are some examples. Both evaluate only accelerometer and gyroscope responses, neglecting cortical and muscular implications, but translating a typical visual inspection in an unambiguous signal. Furthermore, classifications algorithms and evaluations are entrusted to computing units (i.e. PC) in post-processing (offline) mode. eGaIT [7] does not provide useful information about PD's cardinal features (i.e. dyskinesia). Finally, PKG [8] excludes from the assessment the postural instability.

In this frame, we propose a gait cortico-muscular indexes evaluation platform for PD patients. The architecture - fully implemented on Altera Cyclone V FPGA - combines and processes in parallel both electroencephalographic (EEG) and electromyographic (EMG) bio-signals in order to define in *real-time* the modulation of ad hoc calculated indexes to characterize the gait. For instance, the monitoring of these quantitative parameters before and after a treatment allows verifying the degree of effectiveness of the treatment, which is dispensed to the patient. The here proposed Cyber-Physical System (CPS) is an improved version of the system implemented in [9]. Differently from [9], this CPS implements a novel stage for muscular indexes evaluation, allowing precise gait analysis. The platform has been tested on a Parkinson's diseased (PD) patient before and after the Levodopa treatment.

This paper presents detailed results of the above-mentioned in vivo measurements, highlighting quantitative gait modification due to the effect of Levodopa. The structure of the paper is outlined in the following. Section II introduces the basic medical knowledge for gait analysis, focusing on both EEG and EMG evaluation. Section III outlines the CPS architecture and previous implemented EEG-EMG branches. Section IV introduces the new computing block for the patient muscular status evaluation and its implementation on FPGA. Section V presents experimental results. Section VI concludes the paper.

II. The Architecture Background: Previous Work

Exploiting the Cyber-Physical System (CPS) proposed in our previous works [9, 12-14], a new computing branch has been added to the overall architecture, aiming to extrapolate useful indexes related to abnormality in walking pattern, which are typical features of neurological patients as the ones with PD.
Recognizing and quantifying the typical drift in gait alterations indexes (brain or muscular implications) allows to outline the positive/negative effects of a specific drug treatment, and thus makes possible to adjust the dose if needed.
The CPS consists of a wireless body area network (WBAN) linked to a gateway, which collects and on-line processes the EEGs and EMGs signals. The CPS calculates muscular activation and cortical implication flags, for the recognition of voluntary movements.

Medical Background

Before performing a voluntary movement, our brain activates a cerebral process dedicated to the ideation and activation of a proper muscles sequence stimulation. This brain process starts 1 second before the muscle activation. The occurrence of the EEG Movement Related Potentials (MRPs), before the EMG activation, shows the movement intentionality, as well as its magnitude returns an objective evaluation of the cerebral cortex implication in the specific movement. [10]. As in [9], the implemented CPS focuses on three MRPs: Bereitschaftspotential (BP), μ and β rhythms. BP ranges in 2-5 Hz band reaching its magnitude peak about 200ms before the movement onset [10]. The μ-rhythm occupies the 7.5-12.5 Hz band (and primarily 9–11Hz), and can be defined as a kind of steady state of motion. μ -rhythm is suppressed after the motor action [10]. The β-rhythm ranges between 12.5 and 30 Hz. β-waves recorded in the motor cortex are associated with the muscle contractions that happen in isotonic movements. [10]. MRPs are more visible on the motor cortex. In parallel, EMG are processed in order to both evaluate the cortical implication during the movement (extracting a Trigger signal), and to extrapolate muscular parameters (analyzing the Trigger Signal). The synergic assessment of EMG and EEG parameters provides an objective version of the Unified Parkinson's Disease Rating Scale (UPDRS) – III and IV part Score in Gait Evaluation [11], which is a clinical rating scale composed by discrete grading scores from 0 to 4 that allow the evaluation of the motor symptoms in PD. The Section III concerns a general Motor Test, assessing the motor cardinal features of PD subject. The Section IV deals of long-term Motor Complications – nonobjective - inspection (i.e. the assessment of the drug effects during long

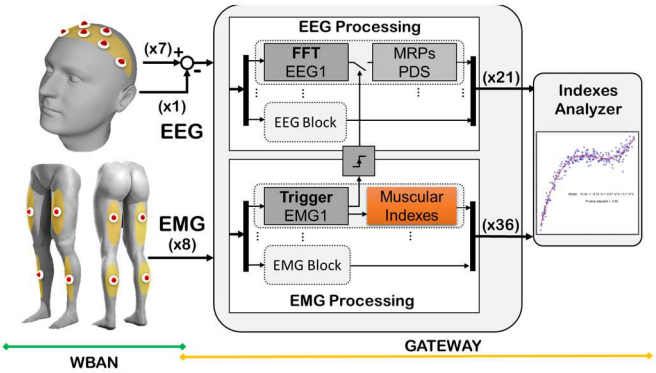

Fig. 1. Architecture of the proposed system. EEG and EMG signals are wirelessly collected by a central unit which includes an implementation of the proposed architecture, here validated on an FPGA.

period is left to caregivers, which must return a precompiled module with personal evaluation of the patient health status). These score are often left to the physicians' expertise.
Aiming to uniform the physicians' evaluation, the extracted indexes are: agonist-antagonist muscles co-contractions, co-contractions Haste Rate (HR), i.e. the number of co-contractions/s, activation and relaxation times for of each single muscle under investigation. The first two muscular indexes, jointly with the MRPs presence/absence, allow compiling the UPDRS-III section related to postural stability and involuntary movement. These indexes (co-contractions, HR, and MRPs) provide significant information about the unbalance, instability and involuntary muscles cross-activation (dyskinesia). The single muscle parameters (activation and relaxation times) contribute to fill of the UPDRS scale in Section III and IV. They allow the evaluation of the bradykinesia degree (i.e. slowness or abnormal muscular hyperactivity). In addition, they allow to objectively assessing motor fluctuations in long period, which are linked to a wrong dose of drug, by using a set of muscle activation/relax timer (known in Section IV [11] as State ON-OFF).

III. The Cyber Physical System

Hardware. The system, outlined in Fig.1, uses 8 EMG electrodes and 8 EEG ones. The EMG electrodes are placed on *Gastrocnemius, Tibialis, Rectus and Biceps Femoralis* of both the legs. The EEG electrodes, according to the international 10-20 system, cover the pre-motor cortex area with T_3, T_4, C_3, C_4, C_Z, P_3, P_4 positions. O_2 electrode is used for noise reduction. The EMG signals are sampled at 500Hz with 16bit resolution while EEG channels have the same sampling rate (500Hz) and 24bit resolution [12-14]. A wireless and wearable recording system collects both the signals and sends them to a gateway. The signal processing is performed in real-time on an FPGA.
Working Principle. The EMG electrode detects the movement, due to a muscle contraction (*Trigger*), and magnitude level overcomes a learned baseline (*Edge Enable*). The trigger enables the computing unit that operates a time-frequency analysis on the EEG data, in the 500ms preceding the movement. The EEG analysis consists of a MRPs detection by using thresholds based approach. The overlap of the dynamic thresholds detects three MRPs flags for each channel – 21 flags in total, identifying the voluntariness of the movement (see Fig. 1). Here we introduce in the FPGA, a novel computation block

with respect to [9, 12-14], the Muscular Index (MI) block, which follows the Trigger generator one (in orange in Fig. 1). It extracts in real time 36 MIs from EMG signals, supporting the cortical implication information.

Algorithm. The movement detection is entrusted to 1-bit trigger signals (one trigger for each muscle) obtained by dynamic-threshold approach [12]. The EMG is stored in an M samples shift-register (M = 512 -1s). The mean value of all register samples defines the global average (GA) and it is used as threshold. A second average is computed on the last *N* samples (with *N<M).* For this local averages (LA), our design adopts *N* = 128 samples (~250ms). Finally, the LA is compared with the GA threshold. Since the threshold is dynamically updated (as soon as an EMG sample arrives), the algorithm allows to follow the trend of the muscular tone continuing to work properly. The EMG trigger stays at high level until the local power is larger than the dynamic threshold. The EEG branch works in parallel with the EMG one. Once a new EEG sample arrives, data are stored in a 256 samples shift register and when a rising edge on the coupled EMG is detected, a 256 points 24bit resolution Fast Fourier Transform (FFT) is computed on the previous 256 EEG (~500ms before the movement). The obtained power levels for each EEG channels are then compared to fixed thresholds in order to evaluate the voluntariness of the EMG contraction. EEG thresholds are subjectively calibrated during a Machine Learning stage [12]. With its high parallelism, between EMG and EEG data, the previous CPS [9] was able to recognize critical situations during gait and to quickly provide (less than 300ms) a postural corrective action.

A. Previous FPGA Implementation: EEG-EMG Branches

The global system clock is set to 8.19209MHz (signal `8 MHz CLK`), obtained with an on-chip Phase-Locked Loop (PLL) from the embedded 50MHz oscillator. The global signals of the whole implementation are: `Reset`, an asynchronous reset, `Enable`, an enable signal which freezes the processing; 500Hz CLK, an input data clock signal from the EMG and EEG channels (500Hz frequency).8 EMG and 7 EEG branches works in parallel on FPGA [9]. The following section briefly summarizes the FPGA implementation of the CPS [9] in order to help the understanding the operation of the MIs block.

EEG Computing Branch. Within the branch there is a 256 point 24 bit resolution FFT processor based on a butterfly structure. The 256 EEG samples to be transformed are dynamically stored in a 256 24bit words RAM addressed by a loop address counter. When EMG `Trigger` rises to `'1'`, the 256 samples stored into the RAM are passed the FFT block by properly temporizing through a series of dedicated states. A MRP Calculator interprets the FFT output data in order to extract the BP, μ and β powers, in natural units (`BP`, `MU`, `BETA` signals). Finally, BP, μ and β are compared to fixed thresholds related to the subject, preloaded on the FPGA [9].

EMG Computing Branch. As shown in Fig. 2, the EMG samples are squared and passed to two blocks named GA and LA FSM. The FSMs calculate the dynamic threshold (`G_Pwr`) and the local power (`L_Pwr`).

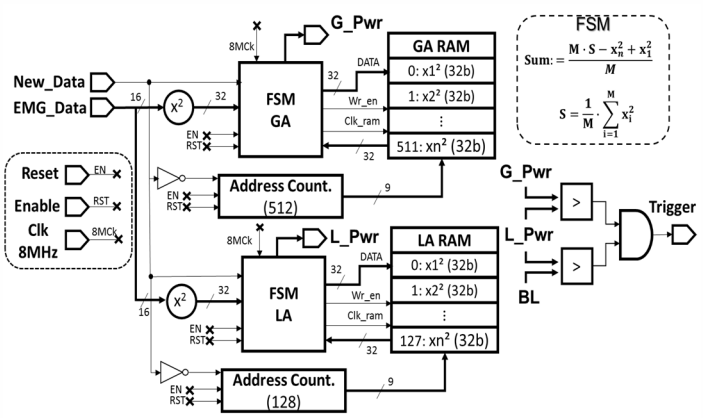

Fig. 2. Schematic diagram of a single EMG branch

Basing on two block RAM (GA and LA in Fig. 2), when a new EMG data is sampled and stored (`New_Data` goes '1'), the last sample, previously inserted, is pointed and "pop" (512th and 128th for `GA` and `LA RAM`, respectively) in a FIFO-like functionality. The read sample is subtracted and the new sample is added to refresh the overall power, `Sum`, within the window. The FSMs overwrite the RAM word with the new data. The 128bit based FSM differs from the 512bit based one, because in the LA `Sum` is divided by 128 (it is traduced in a 7bit right shift) while for the GA by 512 (9bit right shift). A 64bit comparator (`>`) compares the powers calculated by the two blocks (`G_Pwr` and `L_Pwr`). `L_Pwr` is also compared to the learned fixed threshold that prevents uncontrolled activation connected to noisy events (`BL`). The comparator provides a 1bit EMG `Trigger`, used both in the EEG and muscular computing.

IV. Architecture Improvement: the Muscular Indexes

The precision medicine has led to the demand for more objective and on-line assessments of the patient's muscular status. The objective knowledge and quantification of these parameters help identify the stage of the disease and allows to shape a particular treatment accordingly, on the basis of the specific needs. In order to provide quantitative parameters for the complete gait analysis and aiming to assess benefits and side effects of particular treatments (in our application: Levodopa administration), without post processing needs, an improvement on the system was needed.

Referring to the Fig. 1, the MIs branch concludes the EMG block operating after trigger generation through a set of time counter driven by the system clock. In particular, the system generates a first set of 1bit co-contraction signals. A co-contraction signal is obtained by the overlap of two muscle triggers that operate as agonist-antagonist couple (i.e. Left Rectus and Biceps Femoralis). On 8 coupled EMG, 4 co-contractions signals are extracted. The MIs block computes the co-contraction time (number of sample between positive and negative edge of the signal) providing a quantitative value with 2ms resolution time.

The system extracts the HR, counting the co-contractions' peaks during a second of acquisition (512 samples). Furthermore, the system derives three single muscle

contraction time, relaxation time and the step duty cycle. Specifically, the step duty cycle is defined as:

$$DC(\%) = \frac{t_{con}}{t_{con}+t_{rel}} \cdot 100 \quad (1)$$

where t_{con} and t_{rel} are contraction and relaxation times on each muscle, respectively. $t_{con} + t_{rel}$ corresponds to the step time. Signal processing outcomes are stored (for post-processing operations necessity) and real-time displayed to the user (i.e. physician in outpatient applications or caregivers).

A. General features of FPGA Implementation

The architecture has been implemented on FPGA (Altera Cyclone V 5CSEMA5F31C6N) with the future goal of an ASIC implementation [15 - 19]. In our design, 16 bio-signals (8 EEG and 8 EMG channels) inputs and 57 outputs, have been used. The inputs, coming from signal conditioning circuits [17], are serially canalized on 16 FPGA GPIO ports. Finally, they are subjected to filtering and decimation. The 57 outputs, which are functionally distributed on the remaining available GPIO ports, consist of:

- 7 (motor- cortex channel) BP, μ and β 1bit flags (21 parameters), already present in [7];
- 4 co-contraction 1bit signals, already present in [7] .
- 4 co-contraction time values of 11 bit (2ms time resolution on a full scale of about 2s).
- 8 contraction and 8 relaxation times of 11 bit.
- 8 duty cycles with 7 bit (1% resolution).

The need for an immediate response, has led to the development of an interface that allows both the post-processing of the acquired data and the on-line evaluation of the MRPs and MIs (i.e. through a set of displays).

B. The MIs Computing Branch on FPGA

Fig. 3 schematically explain the operation process of a single MIs computing branch. Eight MIs branches are present in the architecture, one for each monitored muscle. It operates serially with the `Trigger` signal, and thus, when the `Trigger` goes '1' the `Contraction Counter` starts increasing its value by 1 bit, every time a `500Hz CLK` positive edge occurs.

A similar operation is carried out on `Relaxation Counter` that is fed by the `Trigger'`. Since a clock of 500 Hz allows a resolution of 2ms, the counters are in "module 2" mode (outcomes are multiplied with decimal 2). When the step is ended, both the counter are ready for the output. Indeed, the loop counter does not reset the `Contra Time` because the `Trigger` signal work as count enable, allowing it to be available in parallel with `Relax Time`. A progressive bit sum realizes the `Step Time`. When the second `Trigger` positive edge arrives (that corresponds to the step time) all the MIs extracted until now are stored and then "popped out" by a 2 pulses based PIPO register, under the piloting of the 1 bit `Reg EN`. A delayed version (two `8MHz Clk` pulses) of `Reg EN` resets `Contraction` and `Relaxation Counters`, in order to allow the data transfer before the asynchronous reset. In this way, all the useful values (`Contra Time, Step Time`) are simultaneously present downstream from the PIPO for the entire next step time.

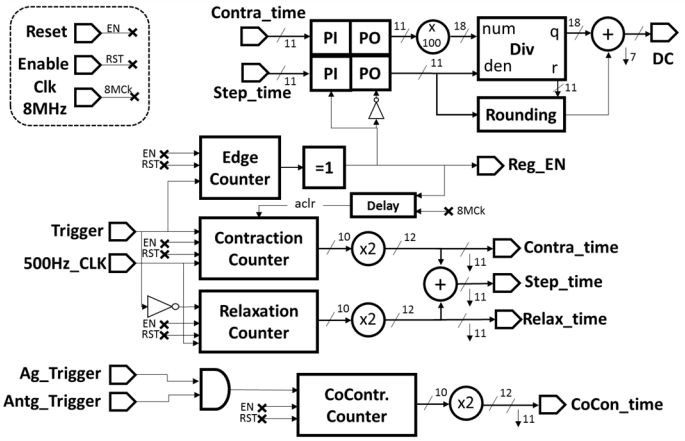

Fig. 3. Schematic diagram of a single MIs branch

This approach isolates the counting section, generating a static calculation section for the DC.

Here, the high level time (`Contra Time`) is first multiplied for 100 (decimal) and then divided by the entire step duration (`Step Time`). The quotient in output represents the integer value of the `DC` (7bit). The remain of the divider block is defined as a binary subtraction between `Step Time` and `Contra Time`. It is multiplied with 100 (decimal) and thus divided for the `Step Time`. If the quotient overcomes 50 (decimal) the `DC` is increased by one. This process halves the error. Agonist and Antagonist muscle triggers jointly contribute, through an AND gate, to generate the square co-contraction waveform. Similarly to `Contraction/Relaxation Counters`, the co-contractions time is evaluated (`CoCon Time`) and returns its value when the step - in which the co-contraction is contained - end.

C. Data Compressing and Output Management on FPGA

Since the overall number of extracted parameters (57) with an output data rate of 2157bps (256bit on 120ms for Single Muscle Param. and 24bps for co-contraction quantification) overcomes the outputs available by the FPGA (24 ports), it has been necessary to compact output data that operates in parallel (`Contra Time`, `Relax Time` and `DC`). The system generates a 32 bit word for each channel, putting in append the values as shown in Fig. 4 under the term "Data Compressing". Analyzing the gait biomechanics through a post processing of all triggers, it arose a timing issue to send the data in output, due to the contemporary behavior of certain muscles (i.e. Biceps Fem. and Tibialis in terminal swing phase of the gait). In order to avoid the congestion on the outgoing data, the output system needs to be synchronized with the biomechanics timing. The system divides the temporization branches into Upper Section for Rectus and Biceps Femoralis and Lower Section for Gastrocnemius and Tibialis. Fig. 4 shows, starting from the top, the sequential muscles alternation for the lower section: Right Gastrocnemius, Left Tibialis, Right Tibialis and Left Gastrocnemius.

In order to minimize the needed RAM blocks and outputs, a synchronized R&W section has been realized. Fig. 4 summarizes the operation referring only to lower section of the

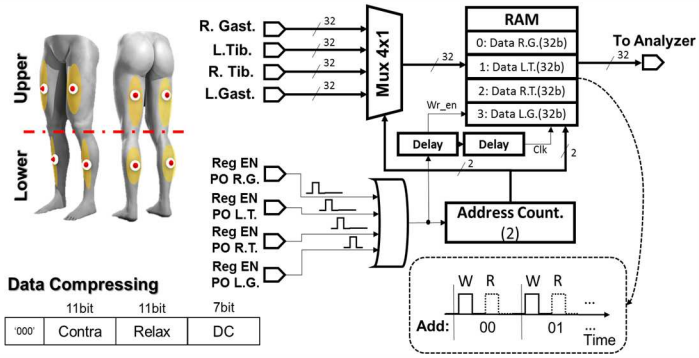

Fig. 4. Schematic diagram for data compressing and output management

legs. The system exploits the `Reg EN'` signals coming from each channel (used for the parallel output process, and thus, named `Reg EN PO`) in order to generate a square waveform, which increase a loop address counter (2 bit). It pilots both the 4x1 multiplexer block and the RAM address. A delayed version of the signal downstream the OR gate works as `Write Enable` (avoiding operation on RAM during addressing edge), and a shifted version of the signal is used as clock for the read operation (dotted temporal diagram). A similar system is used for the upper section, which is based on the biomechanical order: Right Rectus, Left Biceps, Left Rectus, and Right Biceps.

V. RESULTS

In this paper, we present a dataset including EEG/EMG and MIs obtained by a subject affected by Parkinson disease (PD), performing natural gait. The subject is asked to perform a natural and fluid walk in a straight path of 10m for 10 times (5 before and 5 after treatment) within a time range of 120 min, starting from the Levodopa administration. The duration of each gait was about 50 s, interspersed by 10 min. These clinical tests are performed in a controlled environment (local hospital), under the supervision of specialized staff. The assessment regards the short-time impacts of the Levodopa on the patient. The present section provides quantifications of the considered diagnostic indexes. We expect to find only the benefits, linked to the drug, by an assessment in the short time.

A. Cyber-Physiscal System Performance

The overall FPGA implementation uses 28967.5/32070 (90.3%) ALMs, 50177 ALUTs, 48020/64140 (74.9%) registers, 10.3% block memory of the available resources. Table I defines the resource utilization of the architecture. The first entity in the Table I summaries the resources consumption of 8 EMG triggers and 4 Co-contraction signal generation. The second row quantify the MRPs calculation resources needs for 7 EEG. The third entity (Single Muscle Parameters) concerns the utilization concerns the extraction of `Contra Time`, `Relax Time` and `DC` for 8 EMG channels. The fourth subsystem is related to the extrapolation of `CoCont Time` and `HR` for 4 agonist-antagonist couples. The voice Single Muscle Out Management refers to the output data canalization in a single output pin with biomechanics timing, for lower and upper section (Section IV.C). The only MIs system uses 2784 logic elements out of 32070 available, 256/4065280 memory elements RAM and registers 944/64140.

TABLE I. FPGA RESOURCES UTILIZATION

SUB-SYSTEM	ALMS (TOT: 32070)	ALUTS	REGISTERS (TOT: 64140)	MEMORY BLOCK (BITS) (TOT : 4065280)
COMPLETE SYSTEM RESOURCES CONSUMPTION: RESOURCES BY ENTITY				
EMG Triggers Generation	1836.2 (5.7%)	3880	1432 (2.2%)	163840 (4.0%)
MRPs Calculator	23996 (74.8%)	40286	45227 (70.5%)	255164 (6.3%)
Single Muscle Parameters	2657.6 (8.3%)	5264	800 (1.3%)	0
Coupled Muscles Parameters	44 (0.14%)	48	120 (0.2%)	0
Single Muscle Out Management	73 (0.23%)	38	24 (0.04%)	256 (0.006%)
Total	**28967.7 (90.3%)**	**50177**	**48020 (74.9%)**	**419260 (10.3%)**

B. Experimental Results in Gait Analysis

The parameters here reported and discussed are obtained considering the average on first 5 walks as "*Before drug treatment*" status (blue background in Table II), and the 5 final walks as "*After drug treatment*" status (red background in Table II). The results summarized in Table II quantify the muscular implications of the drug treatment in the short time. The Fig. 5 and Table II show:

1. *The maximum co-contraction time is reduced of 23.6% after the treatment.* Before the Levodopa administration PD subject had a maximum co-contraction of 840ms; after the application the maximum reaches 628ms on R. Rect-R. Bic.
2. The HR is, on average, reduced of 23.3% after the treatment. PD subject exhibits 1.92 co-contractions/s and 1.02 co-contractions/s respectively before and after the treatment. *Co-contractions are less frequent in PD after the Levodopa.* Dangerous co-contraction decrease is also highlighted in Fig. 5 with a red circle.
3. The co-contractions show a decrease of 53ms (average value on all the four muscles couples), here with greater incidence on the right leg (Δt=-51ms on R.Gast-R. Tib and Δt=-78ms on R. Bic – R. Rect).
4. On single muscle, the duty cycles follow an opposite trend, showing an average increase of 2.25%. *It represents an increase of the muscular activity during the step* (i.e. due to the stretching in time of the contraction)
5. The contraction time on single muscle is reduced, on average, of 5.4% (576ms→544ms), similarly the relaxation is reduced of 18.8% (546ms→443ms). This behavior is linked to the loss of the slowness status. Indeed, *step time after Levodopa is reduced of 100ms, starting from 1.2s.*

During the gait, significant differences on MRPs were found, showing a reduction of intentionality in the phase of motor

TABLE II. MIS EXTRACTED BY THE CPS

	L RECT	L BICEP	R TIB	R GAST	L TIB	L GAST	R RECT	R BICEP
Coco Max (ms)	496		566		464		840	
	418		396		516		628	
Coco Typ (ms)	312±88		221±90		176±72		334±186	
	282.5±90		170±60		272±150		256±150	
HR (Cocontr./s)	1.04(25/24)		1,25 (30/24)		1,58 (38/24)		1,92 (46/24)	
	1.04(52/50)		1.04(52/50)		1.1(55/50)		1.02(51/50)	
Contra time (ms)	440±130	680±110	616±300	518±172	606±190	502±270	478±232	770±282
	444±108	568±130	613±228	470±272	650±130	552±250	446±200	614±130
Relax time (ms)	558±204	708±422	570±94	494±216	716±390	512±206	588±70	222±120
	642±136	372±222	296±122	466±108	404±144	416±300	540±88	414±266
DC(%)	44	49	52	50	46	50	55	78
	41	60	67	50	62	57	45	60

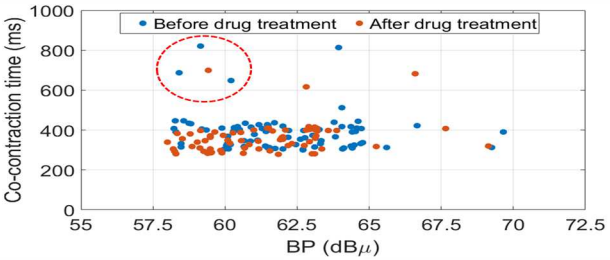

Fig. 5. The co-contraction versus BPs during a gait.

TABLE III. MRPS EXTRACTED BY THE CPS

		T3	P3	C3	CZ	C4	P4	T
MRPs	BP(dBμ)	67.8±8.5	63.8±6.7	62.3±6.7	65.6±13	65.1±7.4	63.8±13	66.2±12
		60.7±6.3	62.3±5.6	62.7±5.4	62.4±5.1	60.9±5.9	62.4±5.2	62.9±5.7
	μ (dBμ)	49.2±2.3	50.1±2.9	49.0±2.4	47.9±9.1	47.0±9.0	52.3±9.5	49.0±9.0
		48.5±2.3	48.9±2.9	48.6±2.7	48.3±2.7	46.6±3.0	49.6±2.7	48.3±3.0
	β (dBμ)	40.1±3.3	41.0±2.8	39.6±2.3	39.6±7.5	40.1±7.2	45.0±4.3	40.8±2.8
		39.31±2	8.9±2.7	37.8±3.2	36.6±3.3	36.1±3.3	41.4±2.2	37.4±3.2

ideation, typical of recurring movements. The decrease is also linked to the parallel decrease of dangerous co-contractions.

Table III and Fig. 6 show the Levodopa brain modulation in terms of BP μ and β rhythm mean and standard deviation of normalized PDFs. The BP before the Levodopa treatment (blue gaussian) has a mean of 64.9 dBμ (average on all the 7 motor-cortex channels) and standard deviation of 9.61 dBμ. After the Levodopa the BP reaches a mean of 62.1 dBμ and a standard deviation of 5.6 dBμ. A relative reduction of 4.3% (2.8dBμ) in BP is recorded. Similarly, the μ- rhythm shows an absolute reduction of 0.8dBμ, or relative one of 1.6% (49.2dBμ±6.3dBμ → 48.4dBμ±6.3dBμ). β-rhythm moves from 40.9dBμ±4.3dBμ to 38.2dBμ±2.8dBμ with a relative decrease of the 6% (2.7dBμ).

VI. CONCLUSION

In this work, a cyber-physical system for gait indexes extraction and computing have been implemented and tested for the evaluation of the short-time effects of the Levodopa administration. The system is made up by 8 EEG and 8 EMG wireless nodes for real-time synchronous data collection. The system calculates 57 different indexes, estimating the cortico-muscular implications during a movement. An FPGA (Altera Cyclone V) implementation, including test and validation of the system has been presented, with a future goal of a more efficient output data management in a long time acquisition (big data issue in indexes storage – 2157bps). The system has been tested on a subject affected by PD, before and after taking Levodopa, performing a standard clinical gait protocol. The experimental outcomes show a situation of benefits linked to the Levodopa such as a reduction in critical muscular behaviors and a modulation of the brain motor ideation, respecting expectations of the drug. The system is therefore highly sensitive to situations such as motor fluctuations associated with bad drug dosages. According to the dictates of precision medicine, this feature makes it a useful tool for treatments evaluation.

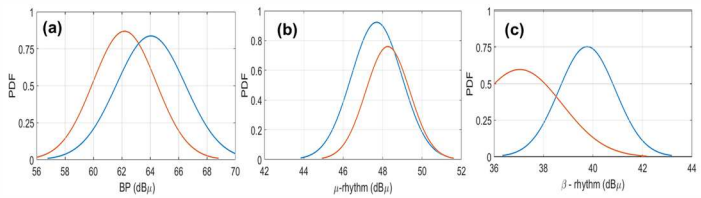

Fig. 6. The MRPs modulation on midline electrode *Cz* before (blue) and after (red) the drug treatment.

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