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Actuator Sub-System: The Auditory Cueing

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7.1 Introduction

Patients with Parkinson's Disease (PD) are usually affected by clinical symptoms associated to a reduced motor performance that frequently compromises their ability to walk independently and safely [1]. While a number of pharmacological solutions help to manage the symptoms of PD, some gait-related problems appear resistant to such treatments and, over time, movement-related disturbances turn out to be the most incapacitating symptoms of the disease [2].

The internal regulation of step length is generally affected, which is reflected as an inability to generate sufficient amplitude of movement, even though the control of cadence, or step rate, is intact. This is in fact the foundation for the use of external rhythmic stimuli, or cueing, as a way to ameliorate the impact of the disease on rhythmic movement-based tasks, as is the case of walking [3, 4].

Typically, to compensate for the reduced step length, patients may increase the stepping frequency. These symptoms are usually referred to as "*continuous gait problems*", since the changes in walking patterns are more or less consistent from one step to the next. With disease progression, "*episodic gait disturbances*" may appear which result in intermittent and occasional episodes, such as start hesitation, Freezing of Gait (FOG) episodes and festination [3–5].

Several cueing strategies, including acoustic and visual cues, can be applied being capable of modifying movements' speed and amplitude, as well as reducing or shortening the occurrence of episodic gait disturbances, such as FOG episodes [2, 6, 7].

Rhythmic auditory stimulation, in particular, enable people to involuntarily synchronize the rhythm of the steps with the rate of the sounds, therefore, enhancing the sense of "taking a step", and the sense of "rhythm", which are both affected by the disease [2, 7–10].

Multiple studies have found a positive impact of the rhythmic sounds on steps length [8, 11, 12], walking speed [9, 10, 12, 13], variability [3, 9] and FOG episodes [2, 14–16]. In addition to the positive impact observed on gait, it was found that rhythmic sounds can also enhance the performance of other tasks involving perceptual and motor timing [17].

Many external cueing approaches are described in the literature; however, several limitations can be identified. Current solutions typically provide interventions continuously (i.e., even when no specific gait symptoms are present), and require cueing to be triggered manually, which limits its applicability in people's everyday life [2]. Also, the application of a continuous cueing means that stimuli are presented without considering whether the patient is suffering from walking problems or not, which can lead to a possible habituation effect that reduces cueing efficacy [18].

To address some of the limitations encountered on previous approaches, an automatic Auditory Cueing System (ACS) was developed throughout the project REMPARK. The developed solution used a smartphone and a headset available in the market, and could provide external cues automatically each time a relevant motor symptom was detected requiring cueing activation. For that purpose, the REMPARK sensor sub-system was used.

This chapter is focused on the Auditory Cueing System (ACS) developed for REMPARK as part of the project implementation. Last part of the chapter is devoted to a technical discussion on the possible future use of the REMPARK developed sub-systems (mainly, the sensor) for an automatic control of the dosage of drug (apomorphine) delivered by an infusion pump, when integrated into the reaction loop around the patient. This technical validation opens the door to future experiences in the way to a better management of the PD symptoms, meaning an improvement on patients' quality of life.

7.2 Cueing Strategies for Gait in Parkinson's Disease

Human beings are particularly sensitive to the temporal characteristics of sound, therefore, *sonification* (generation of data-dependent audio to present information) suits well for time-related tasks, as is the case of the body

movement. Other attributes besides rhythm can also be associated to certain events or processes by listening. Pitch (i.e., the perceptual dimension of frequency), for example, is related to the perceived urgency of a warning and, the higher the pitch, the higher the perceived urgency [19].

Multiple types of sounds were explored by different authors as strategies to guide and provide feedback on walking patterns in people with PD, including, metronome and music. In all strategies employed, rhythm turns out to be a key aspect in influencing time-related tasks, as is the case of walking.

The concept of metronome is generally applied to a device that produces regular, metrical beats with adjustable number of beats per minute (BPM). It is typically used by musicians as a reference to help keeping a steady tempo and was also applied in the context of cueing in PD.

The metronome generates temporal expectations that can be intuitively associated to the cyclic movement of walking. In fact, it allows people with PD to predict when the next step should occur, which facilitates movement optimization and execution [17]. Therefore, it is required that an adequate rhythm is provided to the user, considering his/her normal walking cadence.

The metronome can pace both – right and left – footfalls, by producing a regular, repeated sound at an adjustable pace defined as the number of beats per minute (BPM). Several authors showed that the presentation of sounds with a rhythm that is lower than their natural walking rhythm can be used not only to influence rhythm but also to indirectly influence the magnitude of the movement through an increase in the length of the steps, while maintaining gait speed [9, 20]. A positive impact was also observed in other walking parameters, including the variability of walking [3, 9] and FOG episodes [2, 14–16]. Rhythmic sounds could also enhance the performance of other tasks involving perceptual and motor timing [17].

More complex sounds, including music, have also shown to influence the organization of movement in time and space. Music, like movement, is multidimensional, as such it can be naturally linked to spatial, temporal and force elements of the movement. It can be used as an immediate entrainment stimuli acting during movement, or a facilitating stimulus for training to achieve more functional gait patterns. Music therapists are trained to adjust rhythm, dynamics, and pitch as needed specifically by each patient, according to their rehabilitation needs [21].

Wittwer, et al. in [22] showed that music produced a significant increase in gait velocity in healthy older adults, due to a significant increase in stride length. In contrast, when applied to a group of people with Huntington's disease, and contrarily to what would have been expected, music produced no results, and, in contrast, metronome performed better in this group.

The authors suggested that participants' cognitive deficits may have impaired their ability to discern the beat from the more complex music structure [22].

Besides auditory feedback, other types of external cueing can be applied, including visual and somatosensory cues. Visual cueing is traditionally employed using series of strips placed on the floor in transverse line for the patients to walk over. However, this type of strategy can only be applied in laboratory context, not being useful during the daily life. Portable solutions, such as goggles with light emitting diode (LED) or laser-guided walking canes have been developed, in which the same principles of projecting parallel lines on the floor are applied (see Figure 7.1). Some of these solutions can even present the stimuli on demand, for example, when a FOG episode occurs. However, some issues arise from the use of this kind of strategies in outdoor environments, especially in bright areas where the visual information may become less visible. Moreover, this kind of assistive devices may not be practical for real life usage conditions, due to its obtrusiveness [18, 23].

In addition to these strategies, also rhythmic somatosensory cueing has been explored. Strategies such as electrical stimulation or rhythmic vibration have been studied by different researchers, showing also positive effects on gait [23]. Electrical stimulation, in particular, requires more complex setups that may not be practical for a daily usage [25].

In [23] it is shown that although all the three types of stimuli (visual, auditory, somatosensory) were effective in improving gait velocity, step length and cadence, auditory cueing was in fact the most effective cueing strategy applied. Moreover, it may provide the easiest setup, being more practical and realist for a daily everyday usage.

Figure 7.1   Examples of visual cueing strategies (extracted from [24]).

7.3 State of the Art: Competitive Analysis

A systematic search was conducted on the World Wide Web in order to capture and analyse relevant information about existing studies, projects and commercial solutions, with a particular focus on solutions for auditory stimulation and feedback in PD.

Research included technology being developed and described in published and publicly available papers and conference proceedings, as well as commercial solutions that are already available in the market. Moreover, a patent search was conducted to find out innovative solutions for the management of PD. Search was limited to solutions targeting patients with movement disorders, in particular, patients with PD and technological approaches mostly based on auditory cueing aiming to reduce or overcome motor symptoms related to the disease.

Table 7.1 summarizes the results of said search for R&D and market-ready products. For each solution, the following parameters were evaluated:

- Current stage of development: R&D or market-ready;
- System Components: e.g. smartphone, headset, dedicated hardware, etc.;
- Types of cueing: metronome, music, verbal cueing and possibly others (e.g. visual or sensory cueing);
- Modalities and symptoms: identifies whether a system can or not provide cueing automatically in response to motor symptoms (i.e. the actuation mode); also identifies whether cueing can or not be manually activated under specific circumstances/requirements with the purpose of training (i.e. the training mode); provides a list of motor symptoms that are targeted by the system;
- History Recording, in case the system is able to record the history of activations/deactivations;
- Connection with a Disease Management System (DMS), in case the system is prepared to connect to a server, in which data are recorded to be then displayed and used by clinicians.

Not many non-pharmacological solutions for actuation in PD can currently be found in the market. The majority of the solutions found are still in R&D stage. In particular, related to the auditory stimulation, only one commercial solution was found, the GAITAID Virtual Walker. This solution can provide not only auditory stimulation, but also visual stimulation and for that it requires the use of display glasses with built-in earphones, which are connected to a proprietary control unit that is responsible for creating images and sounds by responding to the user's movements. The system was made in the US, and the

Table 7.1   Technology watch on actuators for auditory cueing in Parkinson's Disease

| | | | Type of Cueing | | | | Features | | | Other Features | |
| | | | | | | | Modalities and Symptoms | | | | |
Solutions	Development Stage	Components	Metronome	Music	Verbal Cueing	Others	Actuation Mode	Training Mode	Motor Symptoms	History Recording	Connection w/DMS
REMPARK ACS [30]	R&D	Android Smartphone, Headphones, Sensor	✓	×	✓	×	✓	✓	Bradykinesia, Dyskinesia, FoG	✓	✓
GAITAID Virtual Walker [32]	Market-Ready	Control Unit, Display glasses with built-in earphones	✓	×	×	Visual cueing	×	✓	×	×	×
iRACE [33]	R&D	iOS-based mobile device	✓	×	×	×	×	✓	×	✓	✓
GaitAssist [34] (Project: CuPID [35])	R&D	Two body-worn IMU sensors, Smartphone, earphones	✓	×	×	×	✓	✓	FoG	×	×
CuePack [36] (Project: RESCUE)	R&D	Control Unit, Display glasses and earphones	✓	×	×	Visual and sensory cueing	×	✓	×	×	×
Bächlin, et al. [2]	R&D	Multiple sensors, Processing Unit and earphones	✓	×	×	×	✓	×	FoG	×	×

prices range from 1995 USD (∼1840 €), for orders in US, to 2145 USD (∼1980 €), for orders outside US and Canada. GAITAID, unlike the REMPARK solution, is not capable of detecting specific motor symptoms, neither actuating automatically upon the detection of the symptoms, being therefore more limited in this sense.

In the study develop by Bächlin, a system for the automatic detection of FOG episodes was developed. For that, they require the use of multiple sensors, which are placed on the waist, thigh and ankle. The system is controlled by a portable processing unit which is placed on the waist and is responsible for processing sensor data and triggering auditory cueing (metronome sound) as soon as a FOG episode is detected. It clearly demonstrates the positive and immediate effects of auditory stimulation in patients' gait.

The iRACE application, developed for iOS, uses the sensors of the smartphone to detect steps and estimate steps length. The finger tapping test is also available in the application. The GaitAssist, which was developed in the FP7 European project CuPID, also uses the smartphone as a support for the execution of physical exercises for training, and enable the detection of FOG episodes through the analysis of the data coming out of two sensors which are placed in the ankles.

CuePack, which was developed in the context of the European project RESCUE, enables the application of different types of stimulus, including auditory, visual and sensory stimulation. Its actuation capabilities are limited to a training context, since it is not able to detect motor symptoms.

According to Table 7.1, no cueing device is as complete as REMPARK ACS. While some solutions are not capable of detecting motor symptoms and actuating accordingly, others, are limited to the detection of FOG episodes. Also, to detect this type of episodes, both solutions require the use of multiple sensors, whereas REMPARK needs just one sensor unit to detect a larger amount of motor symptoms, including FOG episodes, bradykinesia and dyskinesia events.

Some of the presented solutions are based on the use of specific equipment for sounds generation and control, as is the case of GAITAID Virtual Walker, Bächlin and CuePack. In contrast, REMPARK, GaitAssist and iRACE are based on the use of a smartphone.

Moreover, REMPARK can connect to a DMS, enabling also clinicians to analyze their patients' data. As expected, and since the majority of the systems are still in the R&D stage, no references to the connection to a server are usually available in the considered systems.

It was noticed that, to actuate properly, the majority of the systems aforementioned, including REMPARK, require an initial configuration step, in which normal gait parameters for a specific patient with PD are identified and given as an input to the system. This step helps not only to decide when a gait pattern deviates from the normal, but also to establish the functional goals that need to be achieved after cueing is applied.

Regarding the type of sounds delivered to the patients, the majority of the solutions are based on the metronome, i.e. repetitive sounds played with a certain periodicity. REMPARK also offers the possibility of delivering verbal cueing (i.e. "one-two-one-two"). Additional solutions are also capable of providing other types of cueing. CuePack, for example, is able to provide three different types of cueing, including the metronome, visual cueing and sensory cueing. GAITAID Virtual Walker can provide both auditory and visual cueing, which can be used in combination or separately, according to the patient specificities. However, for this functionality, it requires the use of proprietary devices that need to be carried by the patient while walking.

Based on this analysis, and considering the limitations of the current solutions encountered on the literature, REMPARK seems to be the most integrated solution for detection, treatment and management of motor disorders in PD, being capable of actuating in real time, each time a motor symptom is detected and cueing is required. Moreover, it can be used either as a gait training device (at clinics or at home) or during the daily life, at home or outdoors, being capable of actuating automatically when a motor symptom is detected and cueing is deemed as required. As it uses mainly components that already exist in the market, such as the smartphone and a headset, and a single discrete sensor that needs to be worn in the belt, the solution itself may not be stigmatizing for its users, being therefore more attractive.

A more throughout analysis of the existing technology was conducted through the analysis of the patents produced in this area. The most relevant inventions are described in the following paragraphs:

- US 8409116 B2 (Granted, filing date 2010) presented a device and method for treating patients with movement disorders. The device includes a sensor for detecting an akinetic episode (e.g. a FOG episode) of the person and a receiver that automatically issues a single or multiples cues to aid in the restoration of the movement. The cue can be of any type, including verbal, auditory, physical or tactile. Moreover, they propose sending the information about FOG events wirelessly to a caregiver and/or an emergency contact [26].

- EP 2346580 A2 (Application, filing date 2011) disclaims a method for the improvement of gait parameters comprising determining attributes of ideal spatial and temporal gait parameters of the subject, measuring the actual parameters and determining the rhythmic audio cue that may cause the subject to improve a gait parameter [27].
- US 8961186 B2 (Granted, filing date 2012) presents an ambulation accessory that can also be used as a training device. The invention includes two balls that illuminate in an alternating fashion to provide a visual target to each leg. When the user reaches the ball with his foot, the system returns visual and auditory feedback indicating a successful step [28].
- WO 2012177976 A2 (Application, filing date 2012) presents a method performed by one or more processing devices that includes generating a visual representation of an object in the environment, retrieving an auditory stimulus indicative of the location of a virtual target in the environment, determining the proximity of the object to the virtual target and adjusting the auditory attributes based on proximity [29].

As can be perceived, some of these patents describe a system whose operating mode is basically the same adopted by the systems in Table 7.1. They include the possibility of detecting movement disorders, the ideal gait parameters and the cueing strategy/parameters required to overcome said disorder. All the systems described in the inventions offer the possibility of using auditory cueing as a feedback mechanism for gait. US 8409116 B2 presents a generic method that can use just one type of cueing or a combination of several types. EP 2346580 A2, on the other side, is focused on the use of audio cues comprising a tone and a beat. The last two commented patents (US 8961186 B2 and WO 2012177976 A2) are mainly focused on the use of visual cues combined with audio for feedback on gait. As can be understood, these systems lack practicability, as the delivery of visual stimulus while walking requires the use of additional equipment, e.g. display glasses. Systems based on the use of auditory cueing can be largely simpler and affordable, since they can benefit from the use of existing, commercial, equipment that a person may already have, as is the case of REMPARK ACS using standard headsets and a smartphone.

7.4 REMPARK Auditory Cueing System (ACS)

The ACS was developed in the context of the project REMPARK according the specifications and characteristics described in Chapter 3. It uses an Android smartphone, which is connected via Bluetooth to a commercial headset.

The smartphone is responsible for generating cueing sounds, controlling their rhythm and streaming them to the headset (Figure 7.2).

The headset can be any commercial Bluetooth headset with, at least, Bluetooth version 2.1 and A2DP profile [30].

The ACS includes multiple types of sounds, which can be chosen through the smartphone interface. It includes metronome sounds, musical beats, clapping and verbal cueing ("One-two-one-two"). The patient may himself select the sound that he/she prefers the most and is more comfortable with.

Each sound, in reality, falls into the category of a metronome, considering that all sounds produce metrical beats with adjustable number of beats per minute (BPM). The rhythm of the sounds is provided in beats per minute for a direct connection with gait cadence or step rate, also defined as the number of steps per minute (SPM). Both footfalls, right and left, are paced by the system (Figure 7.3), and some of the available sounds are actually a combination of different timbres that aim at providing a different feedback for each step.

The ACS takes advantage of the existing modules that are integrated in the REMPARK solution, including the motor symptoms detection provided by the REMPARK sensor sub-system. The auditory cueing is activated by the system as soon as FOG or bradykinesia are detected by the movement sensor. Once a patient has continued walking without bradykinesia or has stopped walking, the cueing is discontinued. Nevertheless, each time auditory cues are activated, a pop-up window appears on the smartphone screen, for a quick

Figure 7.2   REMPARK Auditory Cueing System.
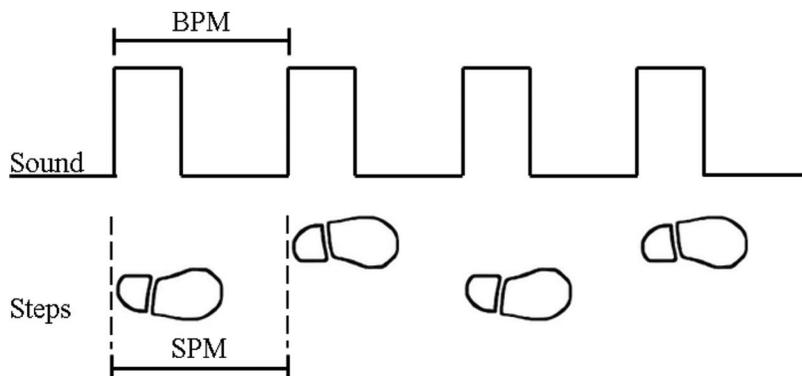
Figure 7.3 Cueing rhythm (beats per minute BPM) and cadence (steps per minute SPM).

interaction with the system, which enables the patient to easily stop the sounds, or manipulating sounds rhythm and volume (Figure 7.4).

The rhythm and volume of cues are pre-configured through the smart-phone. A clinician may introduce the target rhythm for the cueing sounds that will target patients' needs the best as possible. The clinician may also define the maximum and minimum cueing rhythm that can be provided to


Figure 7.4 Pop-Up window for basic control of ACS when it starts automatically.

the patient, so that rhythm may never compromise patients' safety and the safe synchronization of steps with gait cueing, while still maintaining a good pattern of walk. The clinician may also help the patient define the minimum volume accepted by the system, so that it may never go below a level that is inaudible by the patient.

Voice instructions are also available in the system, to explain what to do, or how to proceed each time sounds start playing. Both temporal instructions ("Step in time to the beat") and spatiotemporal instruction ("Take a big step in time to the beat") can be delivered according to the type of symptoms detected. These instructions can be deactivated through the ACS settings application. Through this screen, the patient may also preview each sound available, as well as change the default actuator type of sound.

The ACS can also be activated manually by the patient, and therefore serve as a training device for gait. This will enable patients to listen to the sounds as part of a gait training task. The controller application can be opened from the REMPARK applications list (Figure 7.5).

Moreover, the ACS takes advantage of the capability of recording the history of activations and deactivations, which can then be analyzed by clinicians through the disease management system (DMS) [30].
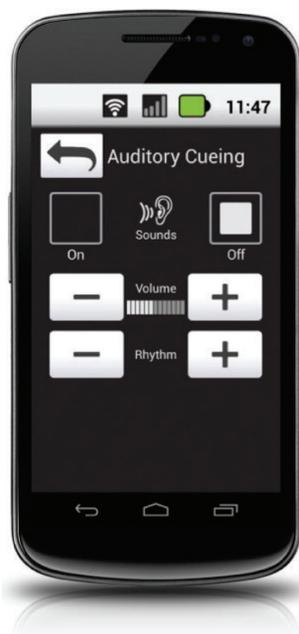
Figure 7.5 Auditory Cueing System application.

7.5 Outcomes from Field Trials: Future Considerations

The ACS was developed as a module capable of providing auditory stimuli in real time, to help people with Parkinson's Disease improve speed and amplitude of walking. Before developing the final version of the system, which was then evaluated in the 3 days-long trials stage, a preliminary testing stage with a first prototype was required to get the first impressions on the feasibility of the system in stimulating gait, as well as evaluate system's usefulness and acceptance.

Preliminary tests were conducted in Spain with 12 people with PD. During the tests, patients were asked to walk, sometimes with cueing, other times without cueing, and their walking rhythm was measured against cueing rhythm. Motor symptoms were identified by observation by a trained medical doctor or therapist. Patients were asked to walk along predefined distances and walking circuits, but also to walk at will, being able to choose the trajectory they wanted to follow. Therefore, both indoor and outdoor conditions were captured (Figure 7.6).

Despite the reduced number of participants in this preliminary testing stage, experimental results suggested that better gait patterns could be stimulated when individuals follow rhythmic sounds whose rate is similar to their natural step rate. The fact that people tended to walk with better walking patterns and overcome gait problems when feedback rhythm was closer to their normal walking cadence supports this observation.

Figure 7.6　Preliminary tests with PD patients for the ACS.

Additionally, people found the volume and quality of sounds adequate, even in outdoor conditions, where a louder environmental noise could be found. This is an important requirement for the system, since it is expected to work in real time, even in outdoor conditions during a person's daily routine. Actually, all participants would be willing to use the system during their everyday life, considering that it would help them in real time during their daily activities. A complete report of methods and results achieved in these preliminary tests can be found in reference [31].

After the final ACS prototype has been developed and integrated with the other REMPARK components, i.e. the REMPARK sensor and the DMS, the final trials period took place, as it is reported in Chapter 9. During the trials, 41 people with PD used the system continuously for three consecutive days and the ACS was put to the test under real life conditions.

After using the system continuously during three consecutive days, people reported some issues related to the size and comfort of the headset. In fact, the headset chosen for the trials was an existing commercial device that was chosen considering mainly its technical specification and price. However, for a final solution, it is also required to consider its aspect, weight, easiness to put and remove from the ear, ear fitting, sense of attachment and sound quality, and take into account also the individual preferences of its users.

In addition, some patients suggested the use of music instead of the metronome to act as cueing during their daily life, to be more enjoyable and not so monotonous. In fact, due to the requisite of maintaining a fixed rhythm, the metronome can become monotonous after a while, therefore challenging the acceptability and sustainability of the solution. Still, it can be the only viable cueing solution for some people, for example, people with cognitive deficits, as suggested by the authors in reference [22].

As a final conclusion, the REMPARK system appears to be usable and participants seem to be satisfied with the system. Improvements on the system will, for sure, take into account the valuable input provided by the people who participated in the trials.

7.6 A Step Further in REMPARK: Automatic Drug Administration

As it has been already discussed in Chapter 3, one of the project goals was to technically validate the feasibility of using REMPARK system to create an automatic or semi-automatic feedback wireless control loop that would

improve the treatment of PD patients, using some reaction solutions. For this purpose, a commercial apomorphine infusion pump was modified. The modifications consisted of incorporating the necessary electronic components so that it is able to communicate with the smartphone in order to receive commands related to the drug dosage to be administered. These commands come from the symptoms' measurements performed by the developed REMPARK sensor. Additionally, the electronic system added to the pump should permit a manual user interaction through the smartphone.

REMPARK project proposal discarded, from the beginning, the organization of a specific pilot action using drug delivery systems control with real patients because this was out of the real possibilities of the project piloting activity. The main reason was the required timing for these type of pilots, where time scales are much more long than those for the rest of scheduled assessment pilots. The only activity, at this level, was to consider the effective possibility of a wireless control of these devices, preparing all the requirements and conditions from a technical and functional point of view.

Apomorphine has been widely used to treat Parkinson's Disease. One of its main usages is under Apo-go Pen format. Doses are small injections which patients can self-administer, with a limited amount of apomorphine. Its active principle provokes, compared to the levodopa effect, a very quick response (within few minutes), and the length of the effect is short, which makes this drug suitable for controlling the symptoms in real time.

At that level, REMPARK project proposed several objectives:

- to technically demonstrate that an automatic drug delivery system can be remotely controlled and activated by the REMPARK system when an unexpected OFF period is detected.
- an automatic delivery of the rescue dose is technically possible.

A subcutaneous infusion pump would be included in the system and would be ready for its automatic activation. This prototype will facilitate functional laboratory testing of the drug delivery pump for remote operation in simulated clinical conditions.

After analysing the existing options, the Microjet CronoPAR [37] subcutaneous pump manufactured by Canè s.r.l was identified as the unique option to be adopted. This commercially available pump provides the functional features associated with the infusion of apomorphine to Parkinson's Disease patients. In order to fulfil the project requirements, an electronic control unit was developed and integrated into the device. Figure 7.7 shows this infusion pump model as it is commercially available.

Figure 7.7   Infusion pump to be adapted for a possible use with REMPARK system.

In the original pump, a set of buttons enable the user to command the behaviour of the pump. A display shows the state of the device. As the device does not have a battery recharge system, the battery must be replaced and it may be accessed removing a side tap.

An automatic control requires the substitution of the manual interaction by an electronic interface, with the equivalent functionality and provided with a connection to the smartphone using a wireless communication channel. The strategy for this modification was to replace the PCB (Printed Circuit Board) integrated in the pump keypad by a much more complex PCB integrating the interaction with the pump, through the electronic control of the buttons, and the mentioned wireless connection.

Figure 7.8 shows the modified Microjet CronoPAR, where the controller has been replaced by a new electronic hardware (PCB). The PCB was designed to allow a similar aspect of the device, with the same functionality and its operative LCD display.

The main directive in the PCB design process was the achievement of a device with reasonable autonomy but keeping the original physical size, allowing the user to wear the subcutaneous pump without undue inconveniences. The components of the system were restricted to be compatible with an adjusted power consumption and practical size. Figure 7.9 shows the general scheme of the PCB device. Internally, the device includes a microcontroller that handles the different sub-system parts. The microcontroller provides the system with the capacity of managing the subcutaneous pump and at the same time to establish a wireless communication.

The control board of the PCB is managed by a microcontroller, which is in charge of controlling the subcutaneous pump while managing the data received from the wireless module. The PCB replaces the original control board of the subcutaneous pump maintaining the same shape, but increasing its thickness.
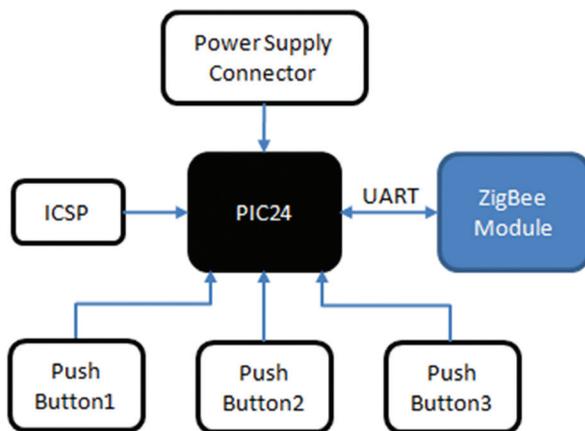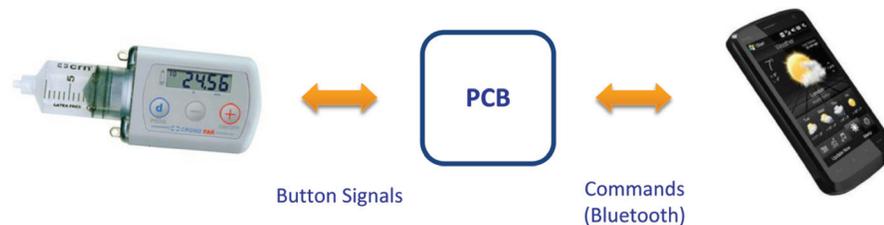
Figure 7.8   Modified pump.

Figure 7.9   PCB general scheme.

In order to control the pump behaviour, the control buttons have been replaced by control signals provided by the PCB. As a feedback, to confirm the proper operation of the pump, an electronic signal associated with internal acoustic information is provided.

The Microjet CronoPAR is supplied with a standard and commercially available 3 Volt type 123 A Lithium non-rechargeable battery with a capacity of 1400–1500 mAh. As the operating voltage range of the PCB is 2.1 V to 3.6 V, it can be supplied with the battery of the original pump. This feature allows

Figure 7.10   System operation overview.

the PCB to work with all the available operating voltage ranges, ensuring that the system can work with any low battery situation.

The control and supervision functionalities of the modified pump are achieved with the execution of the microcontroller's embedded firmware. The system operation relies on a series of independent but coordinated processes that manage the behaviour of the subcutaneous pump, taking advantage of its functional capabilities. The PCB device takes control of the pump behaviour working as a wireless interface between the subcutaneous pump and the smartphone (Figure 7.10). The main state machine (firmware) is in charge of coordinating the commands received from the communication module, giving the necessary functionality to the system and synchronizing the remaining processes. Moreover, the subcutaneous pump provides multiple features (e.g., administration of the bolus dose). These features have been developed as a secondary software (state machine), which is managed by the main firmware software of the device.

It is necessary to confirm that the control of the pump is correctly performed, and also, it is necessary to acknowledge and monitor the correct operation of the device. In consequence, an interface was provided giving the necessary information to the system. This information about the functioning of the pump is provided by means of an electronic signal, associated with an internal acoustic confirmation. Using this signal to complete the feedback loop, the entire system can be managed electronically. As a result, the PCB interface is connected to the subcutaneous pump through four signals: three output signals connected to the buttons of the pump, and one input connected to the beep signal. The connecting diagram between the subcutaneous pump and the PCB can be seen in Figure 7.11.

In order to manage and control the pump, the input signals generated by the front buttons are now provided by the PCB. Then, by activating these signals, the PCB is able to perform all the required actions, for example administer bolus dose or program the infusion rate.
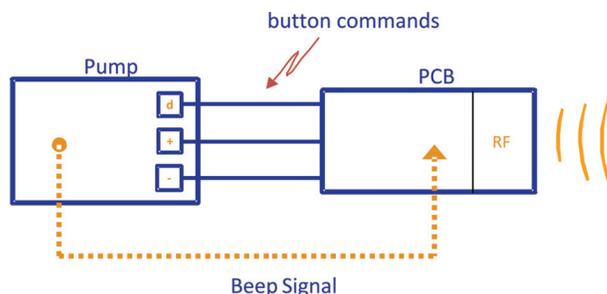
Figure 7.11   Connection diagram between the pump and the designed PCB.

In normal operation regime, the ambulatory infusion pump manufactured by Canè s.r.l. offers two main operative modes: intermittent bolus or continuous apomorphine infusion at variable dose. When operating in a single shot mode the subcutaneous pump administrates a given quantity of drug only once. On the other hand, continuous apomorphine infusion consists on continuous pulses of infusion, where the rate of these pulses depends on the programmed infusion rate.

In REMPARK, the implemented firmware on the PCB is trying to replicate this operative in an electronic way, using a state-machine approach. Deployment of pump behaviour in state-machine based allows a good understanding of the logic process. In principle, the subcutaneous pump has two independent states; *Pump Switched ON* and *Pump Switched OFF*. Each state has the possibility to perform specific actions. For example, the pump must be switched off to program the bolus dose. On the other hand, switching on the pump allows to administer infusion, bolus dose and to program the flow rate.

The OFF state starts when the pump finishes an auto diagnostic routine. Here the bolus dose configuration may be managed. On the other hand, infusion state starts when the pump has been switched on. This state is in charge of managing the main actions that can be requested remotely and mainly the administration of the infusion and the bolus dose. The PCB interprets the command sent remotely and changes the state of the pump in consequence.

To ensure that actions are correctly performed, a feedback from the pump is obtained, as it was introduced. The pump confirms all its actions by emitting a brief sound signal. Then, taking this signal as an input, the PCB is able to read and analyse the action feedback. As a main characteristic, this sound signal has different behaviours depending on the action performed by the pump. For example, the length of the beep signal when the pump changes to infusion mode is different from that generated when it changes to bolus dose

administration mode. Reading and processing this signal by the PCB allows the identification and confirmation of the action performed by the pump at any time.

As it has been already explained, the aim of REMPARK was not to include experience with patients around this implementation of an automatic control loop including the apomorphine pump, but just to demonstrate the technical viability and its feasibility.

The inclusion of a wirelessly controlled infusion pump in the REMPARK system would facilitate some future scenarios:

- If on-line symptoms recognition is done correctly, it opens the door to a better administration of the medication doses, since dosages would be automatically adapted to the immediate needs of patients.
- Usually the practitioner has difficulties for adjusting a suitable dose for the pump's continuous mode, and also to control extra doses administered by the pump. REMPARK can help the professionals to properly assess the number of OFF hours that a given patient has experienced with the aim of judging the effect of the pump therapy through an objective information.
- Usability from the patient's point of view. Some patients with Parkinson's have OFF phases so severe that they cannot even self-administrate extra doses. Patients with severe OFFs, which have no caregivers who can perform this task for them, often cannot choose the treatment with continuous infusion pumps. REMPARK could contribute to improve the quality of life of these patients.

7.7 Conclusion

Current chapter has presented the REMPARK activity on PD actuation as a possible improvement for a more effective management of the disease symptoms.

Auditory Cueing strategy is already a well-known solution for the improvement and facilitation of a better gait of people with Parkinson's when invalidating symptoms appear. REMPARK tries to improve this technique with some new characteristics and possibilities derived from an effective detection of symptoms on-line during the normal activities of the patients.

In a more speculative scenario, REMPARK has demonstrated the technical viability and the feasibility of an electronic control to be added to an infusion

pump of apomorphine, allowing in the future, an automatic delivery of the drug depending on the patient specific needs.

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