

A Concurrent Engineering Approach to Develop BioMEMS Employed in a Deep Brain Stimulator Integrated with a Drug Delivery System

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Abstract. This paper presents an Integrated Product Development (IPD) based model to specifically develop bio-medical micro-electro-mechanical-systems (BioMEMS). The concurrent engineering model is based on the IPD model phases, which are presented and formulated by the Integration DEFinition (IDEF) modeling language. To evaluate the IPD model, a case study concerning the development of a BioMEMS device for a deep brain stimulation (DBS) system was investigated. By following the relevant mechanisms and controls in the model, a design concept of a wireless head-mounted DBS implant integrated with a drug delivery system (DDS) was conceived. The contribution of this paper is the IDEF model, which provides a road map to the product development team members in order to take a concurrent engineering approach to develop BioMEMS. The qualitative feedback received from the identified stakeholders, together with the quality of the case study employed, namely, an integrated DBS and DDS solution, indicate a degree of evidence that the model provides a sound basis in this direction.

Keywords: Integrated Product Development, Design Tools and Methods, Product Miniaturization, BioMEMS

1 Introduction

Physical movement and brain functioning are naturally taken for granted unless a physiological impairment restricts their function. Conditions or symptoms such as tremors, dystonia, obsessive-compulsive disorder, depression, or severe chronic pains definitely reduce the quality of life by restricting these abilities. It is reported by CBC (2010), that one of the most severe diseases which affects both motion and the brain is Parkinson's

disease; a progressive neurological disorder exhibited by seven to ten million people worldwide. It is caused by a deficiency of dopamine-producing cells and affects the motor and coordination functions in a human being.

The monitoring and reduction of tremors associated with Parkinson's disease can be performed through controlled stimulation via a pulse generator device, which can be configured via an external portable programmer. The electrodes, which are embedded in the affected brain zones, receive these controlled pulses and distribute them to the nervous system in order to properly actuate the parts of the body which exhibit abnormal motor activity. This process is known as DBS. In DBS, electrodes are placed in the thalamus or in the subthalamic nucleus or globus pallidus. According to Klaubert (2005), the electrodes are connected by means of wires to the impulse generator implanted under the skin of the chest below the collarbone. A schematic diagram of the DBS setup is illustrated in Figure 1.

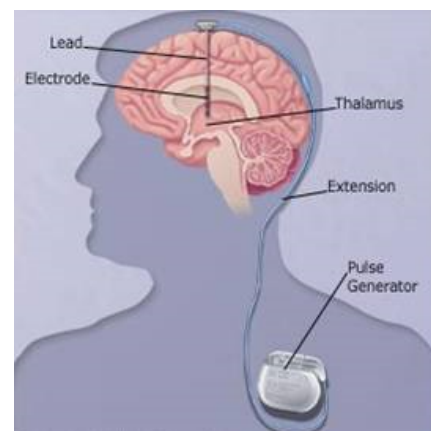


Figure 1: Schematic diagram of a Deep Brain Stimulator (WebMD, 2015).

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Once activated, the device sends continuous electrical pulses to the targeted brain areas, modifying the behaviour of the brain's neural network that is responsible for the motor symptoms. Da Silva (2013) states that this medical procedure is better than thalamotomy or pallidotomy, because DBS can be configured according to the needs of the patient and can be applied without affecting other parts of the brain. DBS is usually supported by means of a prescribed daily drug intake.

Micro-Electro-Mechanical Systems, or MEMS, is a technology that in its most general form, can be defined as miniaturized electro-mechanical elements (i.e. devices and structures) that are made using micro-fabrication techniques. Meanwhile, BioMEMS have emerged as a subset of MEMS devices for applications in biomedical research and medical micro-devices. They are used for various applications such as drug delivery, tissue engineering and bio-sensor development. The study carried out by Da Silva (2013) confirmed that the BioMEMS technology market has been growing extensively in the last couple of years.

In the recent years, automatic drug delivery has been a very active research field in the pharmaceutical industry. Drug intake could be better controlled if the patient has an implantable BioMEMS device that can be actuated in such a way that the drug is released periodically when needed. Although BioMEMS devices provide solutions to challenges faced in the medical sector, they also give rise to a number of issues at the micro-scale level. Alexander, Rogers, Sheehan and Willson (2004) highlighted that one of the most critical issues that has to be taken into consideration when using MEMS devices is bio-compatibility. Any device to be implanted in the body for an extended period of time should not include toxic materials or fluids or pose the risk of causing damage to any local tissue. Another important factor to be addressed is hermeticity, such that the functionality of the device is not compromised by its surroundings. For these reasons, designing BioMEMS is not always an easy task. One should consider various factors in the early stages of the product development, that might affect the final design. The product development of BioMEMS based medical devices has a complex nature since it involves multidisciplinary stakeholders such as physicians and engineers, often with conflicting views (Santos, 2013).

In addition, the development of medical devices is highly influenced by the regulatory requirements and business considerations (Santos, 2013). Despite these challenges, a study by Linehan, Paté-Cornell and Yock (2007) reveals that there was little data on the development process of medical technologies. The findings in this study have also been confirmed by an extensive literature review carried out six years later by Santos

(2013). The IPD model is one proposal for the implementation of concurrent engineering in the product development process (Andreasen & Hein, 2000). This model follows the idea of parallelizing tasks which are carried out by various streams within the product development process in order to allow for concurrent consideration of the problems. In view of this context, the overall goal of this work was to develop an IPD based model specifically targeted for the development of BioMEMS. Given the complexity to develop a BioMEMS device which requires multidisciplinary expertise, modelling of the process will greatly help IPD stakeholders to visualise the information flow from the concept to the product launch. To this end, in this paper the Integration DEFinition (IDEF) modelling language is deployed to portray the various features characterising the information flow in such an IPD model.

Based upon this introduction, the rest of this paper is organised as follows. Section 2 reviews concurrent engineering approaches as well as existing products related to DBS, which are readily available on the market. The developed IPD model is then presented in Section 3, with particular emphasis made on the product design phase. The subsequent section focuses on the implementation of the developed model via a case study of an integrated DBS system equipped with a drug delivery mechanism. Results of an evaluation carried out with a sample of subjects, consisting mainly of IPD stakeholders, patients and neurosurgeons, are presented in Section 5. The strengths and weaknesses of the proposed model together with those of the case-study solution are discussed in Section 6. Further research directions are also proposed. Finally Section 7 draws key conclusions, highlighting the contribution made in this paper.

2 Related Work

2.1 Product Development Models

This section first reviews generic product development models, followed by specific ones, in particular those related to medical devices. Amongst several existing models, the model proposed by Eppinger and Ulrich (2011) starts by the planning phase followed by concept development, system level design, detail design, testing and refinement and production ramp-up. At each phase, marketing, design and production activities are identified. Similarly to the model presented in Andreasen and Hein (2000), these two models are characterized by a matrix which chronologically shows the different development phases in relation to the functional core disciplines (Schätz, 2006). Common to all the aforementioned models is the fact that the information flow between the different phases is not modelled formally using the IDEF modelling language but rather by means of block diagrams and flowcharts (Fenech & Farrugia, 2014). In

this work, the IDEF0, which is one class of IDEF modelling languages, was chosen to model the IPD as it is specifically designed to represent the activities, actions and decisions of a 'system'. Furthermore, apart from its simplicity, the major benefit of using IDEF0 is that it applies dynamic information into the model to handle problems involving parallel activities (Fenech & Farrugia, 2014).

As will be described later on in Section 3, the model presented in this paper is closer to the original standard IDEF0 modelling language, with the introduction of a data connectivity type to reflect the stakeholders input. An extensive literature review of product development models, specifically targeted for medical devices, was carried out by Santos (2013). Over thirty models were reviewed, none of which specifically treated BioMEMS. Watty and Binz (2005) presented a proposal for MEMS design methodology based on the VDI guideline 2206 (Beuth, 2004). Even though this methodology covers the whole life-cycle of a component, it does not specifically mention very important aspects for BioMEMS, which are the need for safety, risk assessment and quality considerations.

Due to the novelty and nature of the products, materials, risk and quality assessment and manufacturing technologies, the development of BioMEMS requires a structured development process. As explained in Smith (1997), BioMEMS need not only efficient components but also their correct and reliable interaction to fulfill the function of the entire system. Despite this, the above review suggests that there exists no definite methodology tailored specifically for the development of BioMEMS. Many disciplines use approved methodologies for product development such as the VDI-guidelines for mechanics as explained by Reichl (1994) and mechatronics as discussed by Beuth (2004), or widely automated design procedures in microelectronics. The models reviewed are aimed at serving as a guideline to implement product development related principles in certain disciplines and do not sufficiently include the interdisciplinary and system interrelations demanded in the development of BioMEMS.

2.2 Review of Deep Brain Stimulation Devices

There are various solutions available on the market for DBS systems. Current systems involve the need for DBS to use electrical impulses to stimulate a target area in the brain which affects movement by altering the activity in that region. The procedure does not destroy any brain tissue and stimulation can be changed or stopped at any time. Some of the solutions are readily available on the market, like MedtronicTM devices, while others are still at a concept stage. It is vital to mention that undergoing DBS surgery does not mean that one stops daily drug intake.

Current solutions offer various advantages such as the fact that DBS is reversible and the patient can stop treatment at any time. DBS can be customized to the patient's requirements in such a way that the electrical stimulation is adjustable according to the patient's response to medications. On the other hand, failure of the battery could result in the device not working beyond its estimated time limit. As a result, this would entail the need for another minor surgery to replace the battery. Also, if the frequency and the intensity of the pulses required by the patient are increased, these could result in the need to change the battery before its expected life-time.

Most common DBS systems generally have the pulse generator system placed in the chest area and which is connected via an extension wire to the electrode region in the skull area. The literature review presented in Cutajar (2014) shows that the device is susceptible to have broken leads or wires, especially the extension wire. This is most likely to occur in slim people. Possible studies could exploit alternative ways to avoid this failure. Research has been made on ways how to extend the battery lifetime of a DBS system. For this reason, seeking to further investigate battery longevity would be a major requirement demanded by the stakeholders.

Current DBS systems are relatively modular, however, if one simply focuses on their function and their additional potential capabilities, one can easily note that it is quite limited in terms of flexibility. This can be mainly noted since its purpose is solely intended for the treatment of uncontrolled diseases or movements. In addition, through an existing literature research (Obeso et al., 2001; Parkinson's Disease Foundation, 2015) it was revealed that while medication is significantly reduced after surgery, the body still needs to be sustained by the daily medication dosage. In addition, the literature survey presented in Cutajar (2014) showed that the integration of these two systems (DBS and DDS) together is in its infancy. DBS and DDS are presented as individual solutions for different purposes.

Through quantitative data gathering from a market research, it was discovered that the currently available pulse generator devices embedded in the chest area are quite large in size (Cutajar, 2014). This possibly results in certain level of discomfort to the patient. The possibility of miniaturization of an integrated DBS system was especially highlighted by young patients (Cutajar, 2014). Based on existing research current systems the current minimum size is approximately 54 mm by 54 mm and the target size is to go down to 25 mm by 25 mm which is approximately half the size of current system. The aspect of miniaturisation combined with the lack of integration of the DBS with DDS mentioned above, provided scope and motivation for the research team to seek an innovative solution.

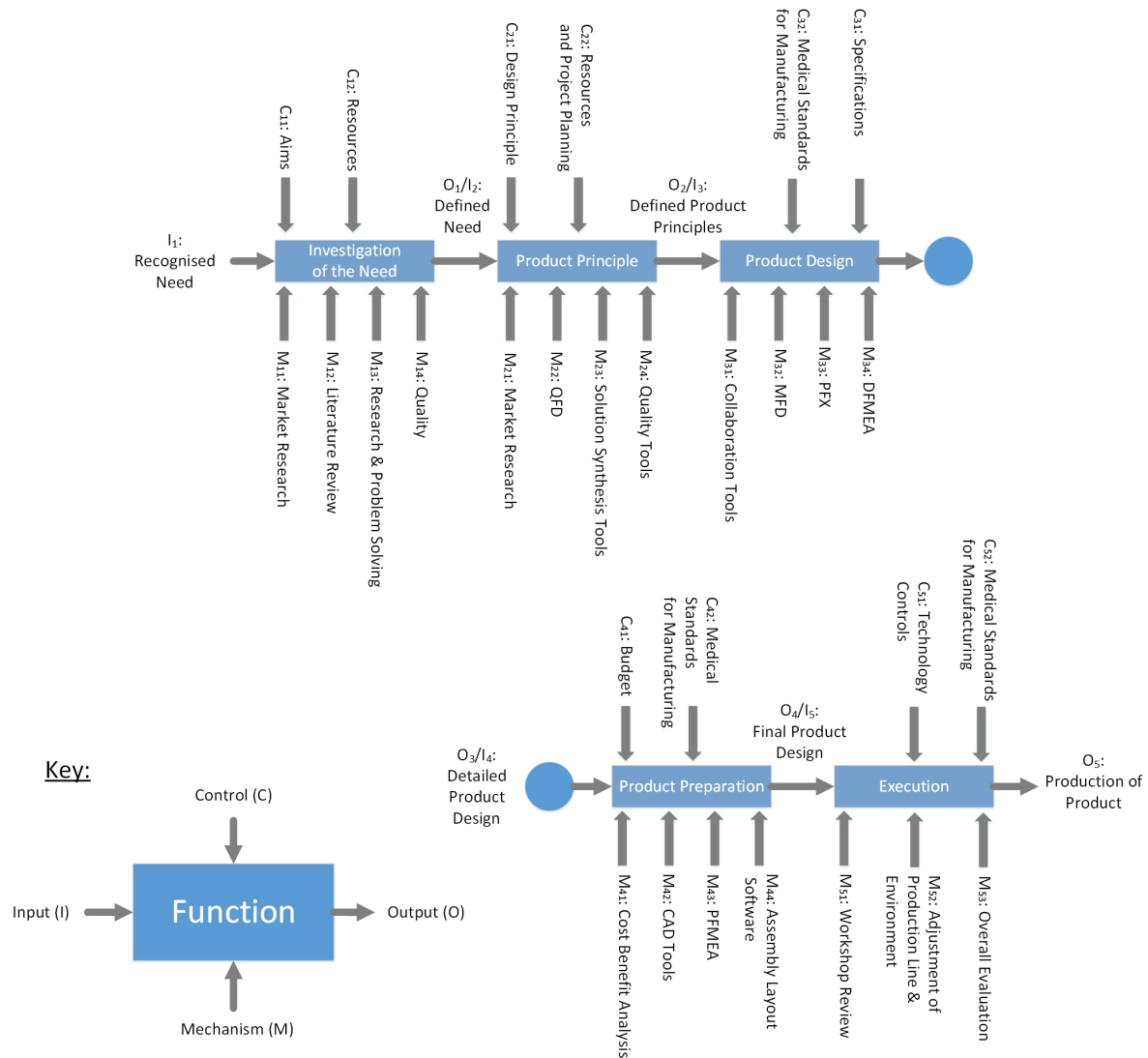


Figure 2: General block diagram of the developed IDEF0 model.

3 An IDEF0 Model for BioMEMS

From the identification of the market gap and the requirements set out by several stakeholders, it is important to formulate a concurrent engineering approach to develop BioMEMS. This new approach needs to make use of a model which provides means for new marketing and sales opportunities while resulting in a planned manufactured strategy to produce high quality products, which conform to the biomedical standards and directives set out by the medical sector.

The model being proposed (refer to Figure 2) incorporates both the IPD model phases such as the investigation of the need and product principle by Andreasen and Hein (2000) and the IDEF0 modelling language principles. It must be mentioned that the phases in Figure 2 can also be perceived as functions within an

IDEF0 modelling context. Andreasen and Hein's model has been employed in this research, since it integrates all the pillars from the very initial recognition of the need to the final execution. On the other hand, a shortcoming of this model and which is addressed in this work, lies in the fact that no explicit reference is made to quality considerations. Through extensive market research it was established that quality is significantly important when developing BioMEMS (Cutajar, 2014).

IDEF0 was chosen as it offers a structured representation of the different functions of a system and it captures the activities, decisions and actions taken. The tool acknowledges that a successful systems development requires input and validation from the users. In fact, IDEF0 incorporates inputs, outputs, controls and mechanisms for a specific function (refer to legend in

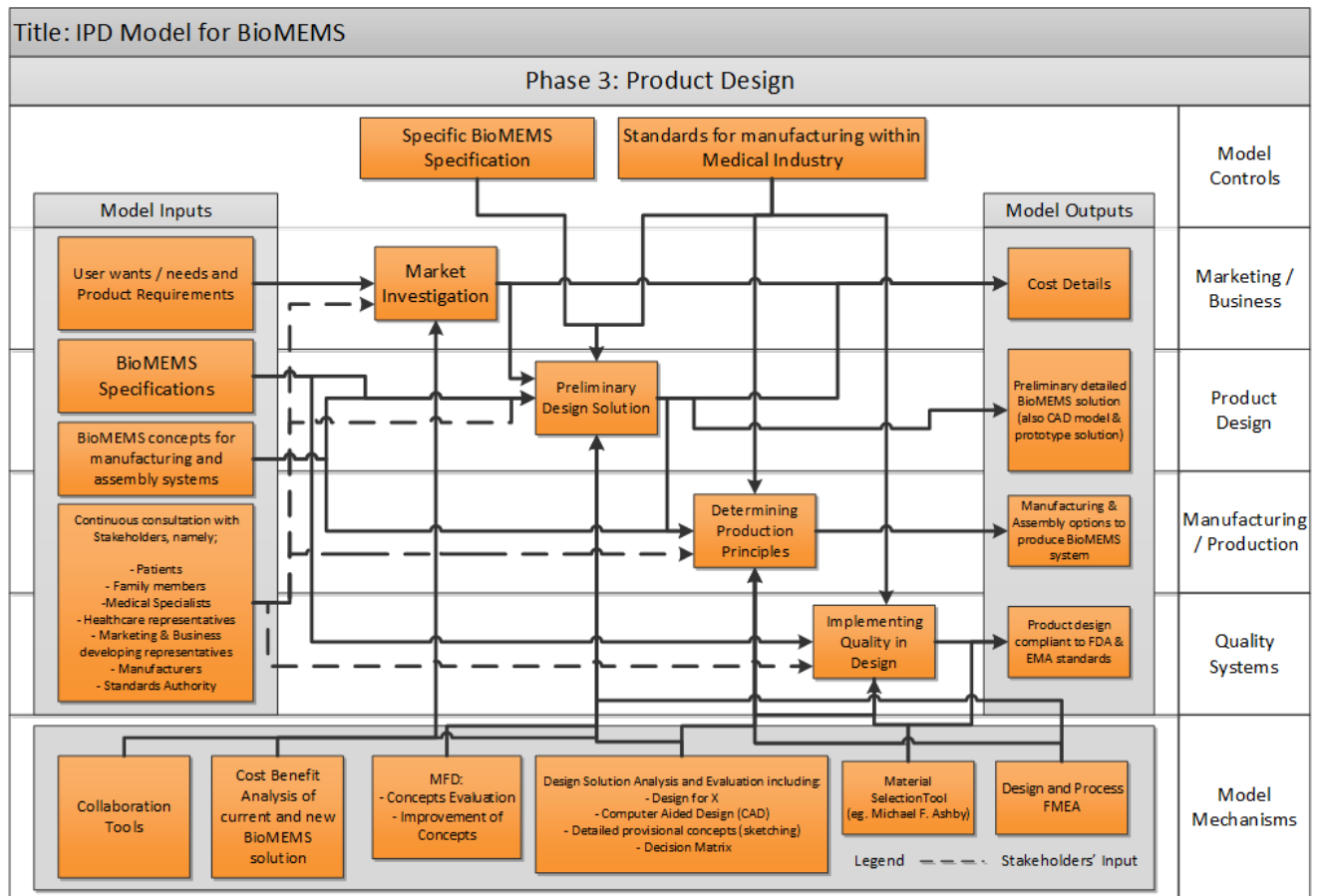


Figure 3: IDEF0 model of Phase 3: Product Design.

Figure 2). It must be pointed out that the IDEF0 model presented in this section was developed and based on the requirements to market, design and fabricate BioMEMS. Figure 2 depicts a general overview of the developed model, consisting of five phases (Phase 1 to Phase 5), whereby development flows sequentially through these phases whilst, in each of these phases, development activity will be taking place both sequentially and concurrently, involving the three IPD pillars along with quality. Since the design stage is critical in the overall IPD model, this paper focuses on Phase 3. This phase involves important decisions on the preliminary design solution of a BioMEMS device and is presented in Figure 3. Further details on the other phases are available in Cutajar (2014).

Phase 3 focuses on the details of the developed concept and the means how to actually produce the first simulation models specifically designed for BioMEMS (refer to corresponding IDEF0 model in Figure 3). As can be observed from Figure 3, the inputs of Phase 3 are fed from the outputs of Phase 2. With reference to Figure 3, 'market investigation', 'preliminary design solution' and 'determining production principles' are il-

lustrated as concurrent activities in the Andreassen and Hein's IPD model under the product design phase. The fourth function regarding quality was added in the proposed IPD model. The primary goal of this phase is to define further design details and ensure that the final detailed design solution is augmented with the stakeholders' feedback and requirements. This is defined in order to enhance the product specifications and set the BioMEMS concepts for the manufacturing and assembly systems. The preliminary design together with the initial considerations of manufacturing systems give rise to the possible ideas and concepts of how the system will be produced.

The mechanisms defined in Phase 3 include, the cost benefit analysis of the new BioMEMS device over current systems and the modular functional deployment (MFD) which is closely related to Quality Function Deployment (QFD). In addition, a number of design modelling tools (e.g. CAD) and design analysis tools (e.g. DFX) and evaluation tools (e.g. decision matrices and material selection tools) feature as mechanisms in Phase 3. To detect any potential weaknesses in the design and subsequently in the process, the Failure

Mode and Effect Analysis (FMEA) tool is also included as a mechanism in this phase. Similarly as in Phase 2, another important mechanism relates to the collaboration tools which aid to facilitate communication between the different IPD stakeholders. For instance, collaboration tools can be used to collectively investigate the market and to determine product principles. At the initiation of Phase 3, the market research would have been carried out, whereby this data would have been gathered and the customer's needs identified. Other controls also include the standards for manufacturing within the medical industry such as the bio-compatibility of the chosen materials which need to abide by the medical standards, such as the Food and Drug Administration (FDA) and European Medicines Agency (EMA) standards. This shall also lead to enhanced concurrency in the development of BioMEMS. One of the major outputs is the need to set out a preliminary design which is carried out by making use of various CAD software tools. It would also be ideal if as an output of this phase, one identifies the possible technologies needed for the production of the components or systems.

4 Application Case Study

To adopt a user-centred design approach, typical end-users of the device were involved in the case study. These included five patients whose age varied between 4 to 60+ years and two neurological surgeons. Due to the difficulty in accessing BioMEMS and integrated circuit designers, it was not possible to engage such stakeholders. The study was carried out by organising different focus groups which were aimed at gathering qualitative data. The case study revolved around the development of an integrated DBS and DDS system. The need for such a system emerged after the patients and the medical specialists highlighted that the patient still needs to take a daily drug dosage after undergoing surgery. The clinical need to maintain medication is generally related only to the non-motor symptoms of the disease. As discussed in Marek and Antle (2008), specific patients have also mentioned that the daily dosage imposes a certain level of dependence on the family members and highly depends on one's health. The fact that patients need to depend on others in order to take their medication is seen as a reduction of one's quality of life. This solution would most likely aid patients who suffer from dementia and similar mental sickness. Many of the risk factors related to inadequate medication management are more prevalent in older adults, like for instance the possibility of mixing prescribed medication which could lead to serious consequences.

During the design phase it is important to determine how the product will be configured. It is also important that the designer keeps into perspective that the chosen

materials conform to the medical standards, in order to ensure that the final device is bio-compatible due to the sensitivity of the environment in which it will be embedded. The various stakeholders were asked about their requirements, in order to be capable to translate these into product design specifications. To this end, a QFD was compiled during phase 2 of the IPD model (refer to Figure 2). The weight distribution of the QFD engineering requirement scores revealed that the most critical requirements of the DBS system include:

- Minimizing the probability of a defective extension wire between the pulse generator and the electrodes.
- Maximizing the patient's comfort – this is very important so as the DBS can be implanted in patients of all ages, therefore, it is crucial that the design of the DBS should aim to maximize comfort. This comes about with the possibility of miniaturizing the device.
- Maximizing battery longevity – this is one of the main critical features in the pulse generator. The better the battery's capacity, the longer the battery lifetime. The procedure to replace this requires a minor surgery. This is something one cannot do without unless the batteries are rechargeable. Thus, it is advisable that at this phase of the IPD model, the latest rechargeable batteries available on the market are sought, in order to guarantee the maximum possible lifetime of the system.
- Need for DBS system to be bio-compatible – it is one of the most important requirements of any medical device which needs to be implanted in the human body.

The results also showed that 60% of the interviewed people state that if they had to choose, they would pick a system which is aesthetically more appealing and less visible. Based on this analysis, this concept has to be unobtrusive. Meanwhile, this device also seeks to incorporate the need for automatic daily drug intake, which could ultimately allow the patients to lead a better lifestyle. A number of concepts were generated in Phase 3, by means of sketching and other synthesis tools, namely morphological charts. These concepts included a range of different configurations of the DBS implant and the DDS. Relevant stakeholders, in particular neurosurgeons and engineering personnel were involved to select the most plausible configuration, through a decision matrix. However, since in the scope of this work the actual prototype was not developed in a real industrial context, certain mechanisms such as collaboration tools, were not deployed during the evaluation exercises. It resulted that the preferred configuration would be a wireless head mounted DBS implant with a DDS. This system would be responsible for two functions, primarily

injecting a designated amount of charge into the human body by providing a precise amount of output current or output voltage for the predefined period (architecture of the DBS is shown in Figure 4(a)).

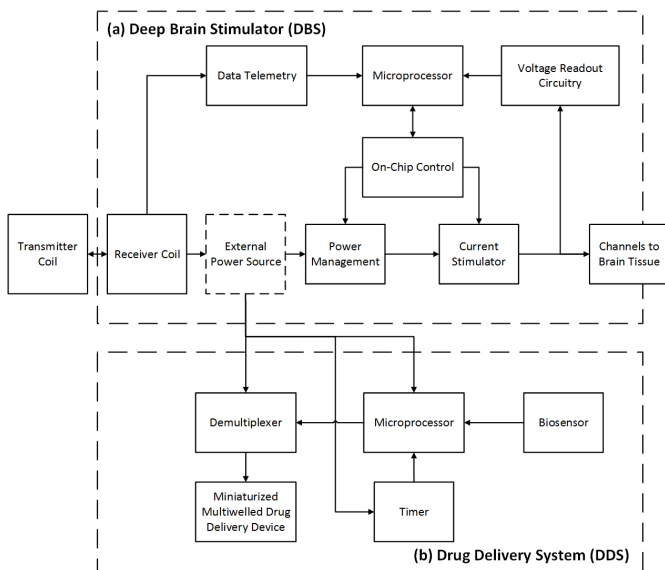


Figure 4: (a) Block diagram of the integrated DBS with adaptive power supply control and active charge balancing for both power-efficient and safe current stimulation (Lee, Park & Ghovanloo, 2013) (b) Architecture of the proposed DDS (Cutajar, 2014).

Secondly, it releases the right amount of drug at the right time needed by the body (refer to Figure 4(b)). These functions may be programmed and configured wirelessly through the use of an external device via a coil (Cutajar, 2014). The same system is used to recharge the in-packaged battery which is chosen to be a non-cytotoxic rechargeable one. An external rechargeable battery energizes the implanted device, which is placed behind the ear similarly to cochlear implants and hearing aids, via an inductive power transmission charger. This would be designed to be removable once the internal DBS system is fully charged. The external battery of the programmer and charger can then be energized 'offline' without being worn by the patient. This presents a well-designed aesthetic, safe and modular device to the end-user and it is quite unnoticeable.

5 Evaluation

As part of the evaluation strategy a number of stakeholders were questioned in relation to the validity of the IPD model as well as the developed device solution. Due to the sensitivity of the subject and the limited availability of stakeholders in the local sector, the sample of respondents was relatively small. In fact only fourteen participants took part in the evaluation process. The results focus on a qualitative rather than quantitative data collection. The participants who volun-

teered in the evaluation exercise consisted of four academics coming from three related fields of study (material processing, neurology and marketing), two neurosurgeons, one neurophysiologist, five patients of different age brackets, one member of the European Parkinson's Association, and one consultant in a company which supplies medical products. The participants were asked a set of questions and presented with the prototype solution and the IPD model in the case of academics. A five-point Likert scale was used to measure the participants' attitude to the posed questions. A selection of the gathered feedback together with sample comments quoted from different stakeholders coming from different sectors are provided in Table 1 (on page 8) and Table 2 (on page 9).

6 Discussion

This section discusses the strengths and weaknesses of the IDEF0 model as well as those of the case study solution which were identified from the qualitative data collected. The degree of validity of the research results obtained is also discussed in the last part of this section.

6.1 Strengths and Weaknesses of the IDEF0 Model

A number of strengths of the IPD model have been identified from the qualitative data collected, namely:

- Since the three pillars of IPD are included as activities in each phases, the proposed IDEF0 model, reflects concurrent engineering, which automatically demands an improvement in the communication between the different departments. In addition, it emphasizes the vertical integration across the three IPD pillars in conjunction with quality considerations (this also includes the risk assessment and safety considerations). This direct relationship accentuates its importance and interconnection. In addition, such integration ensures that a product of good quality is being carefully manufactured according to the exact requirements of the stakeholder.
- The investigation of the need in the early stages of development links to determine the type of product. This would then set targets for the considerations of the process type and the quality systems to be considered. This activity will aid the organisation to decide whether the project should proceed or put on hold.
- The model emphasizes the need to consider quality considerations, safety, risk assessment as well as the importance of implementing standards and guidelines since the device has to abide by a high level of medical standards.
- Activities concerning manufacturing and the possible available technologies are presented in the very

early design stages so that any defects or barriers are highlighted as soon as possible in the design cycle.

- The model provides a visual representation of the process flow along the product life-cycle from the idea initiation stage to the realization which challenges the inputs and controls.
- The feedback implemented in the model permits to revert to particular activities during the development process. Its importance comes about since a minor mistake at the development and production

stage could ultimately result in challenges later on during the product's life-cycle. This may potentially result in high losses for the company.

On the other hand, one of the major criticisms highlighted by the medical team and the business representatives, was that whereas within the IDEF0 phases, a parallel flow is emphasized, reflecting concurrency of IPD, the phases themselves are sequential in nature. This is attributed to the fact that certain inputs emerge from previous output activities.

Table 1: IPD Model: Selection of the qualitative evaluation results and average ratings obtained (1:Bad – 5:Good).

Question	1	2	3	4	5	Additional Comments
Do the IPD pillars adopt a holistic approach and a level of continuity between phases?					X	Marketing and sales are the least important from the IPD pillars since if one is offering a good quality product, one does not necessarily need to market it since patients still believe in the product and need it. For this reason the sales factor is not so important when it comes to such medical products. Having said that, marketing and sales could be one of the main key barriers to certain selective patients. Neurosurgeon The most important pillar is design, as it is the fundamental fulcrum on which any project kick starts its process development. Consultant at a Medical Device Company
What is the level of importance the different solutions (current and new DBS solution) give to the three IPD pillars together with the quality factor?				X		The most important factors are the following: a very good design in the initial stages of the product's lifecycle, a good manufacturing procedure, in order to have one of the best solutions on the market, followed by a good quality product, which abides by the necessary medical standards in this field. The current solution which is available on the market does not cater for good integration between these, however the proposed system takes into account all factors, and meanwhile, one can still improve the sales execution. Neurophysiologist
What is the level of importance given to the vertical integration between the three IPD pillars and quality factor?					X	Vertical integration between the pillars and quality is missing in the currently available devices, and encourages the need for further parallelism between the three pillars and quality, if one needs to achieve a successful product. Neurosurgeon
What is the practicality of the model and does this provide enough tools to address the situation from three different IPD pillars together with quality?					X	If the mentioned tools and methodology had to be adopted during the life-cycle of the process development, the solution to the device would be based on the customers' needs and requirements while ensuring a successful sellable product. Neurosurgeon

Table 2: New DBS-DDS Solution: Selection of the qualitative evaluation results and average ratings obtained (1:Bad – 5:Good).

Question	1	2	3	4	5	Additional Comments
To what extent does the new design address the market gap?					X	The new design offers a safe quality product which provides a safe mindset to the customer. Its miniaturized system can make the customer instantly comfortable. Its size and charging system instantly gives a better frame of mind that it is designed for patients of all ages. This product highlights the voice of the customer. Patient - Parkinson's Disease (Age: 35)
To what extent do the stakeholders benefit from the new design, and how much does the design address the current limitations?					X	The main limitations are usually highlighted via the customer requirements. This was dealt with efficiently. Neurosurgeon Main burden is that the patient constantly needs to remember to take one's medication. This is something which was resolved through the use of the new DBS design. Patient (45 years)
To what extent does the new design address the importance for miniaturization and that of extended battery life-time?				X		The system definitely presents an improvement over the current solution. It deals with the main weaknesses of the systems currently available on the market and addresses these issues in the most prominent way. Patient (55 years)
What is the level of importance given to the new design to address biocompatibility and abide by the regulations and standards for medical devices?					X	The new design ensures that the product is of high quality and abides by the medical standards and regulations. The material selection was carefully selected so as to opt for the best solutions. Lecturer in Materials and Metallurgy
How beneficial is the integration of the pulse generator device and DDS designed as a single system? To what extent does the device offers design modularity to patients to make their life easier?					X	The new system is a single device which caters for different functional solutions, thus offering a level of modularity to the patient. It would be a good idea to have the possibility of two separate solutions. Patient (49 years)
Does the new generated solution present a challenge to implement such device in production?				X		Manufacturing this device is not too complex. The most challenging of all is the nature of the product. The fact that it is a biomedical device, it needs to conform to certain strict requirements. Member-European Parkinson's Association
Do you think the new solution will present a life style improvement?					X	Confident that our lives will be improved drastically. Patient (6 years)
Do you believe that this solution would be cost effective?				X		It will not be a cheap solution especially because of the integration of the new DDS and working mechanism of the wireless rechargeable battery. But it offers a more flexible solution which better caters for the patient's needs. Member-European Parkinson's Association

6.2 Strengths and Weaknesses of the Case Study Solution

The comments gathered from the focus group shed light on a number of benefits of the proposed design when compared to the current design solutions, particularly:

- Improved comfort – a miniaturized solution which can be directly implanted and fitted into the skull area, with electrodes that are implanted in either the subthalamic Nucleus or a section of the globus pallidus. These brain sites normally play crucial roles in regulating movement. This presents various challenges due to the sensitivity and space limitation; however, one of the main benefits is that the device is much smaller and thinner than the currently available systems on the market. In addition, a miniaturised DBS-DDS system will be more appealing to young patients diagnosed with Parkinson Disease, thereby increasing the market potential of the device, given that there is more evidence pushing in the direction of an early stimulation approach (Schuepbach et al., 2013).
- Elimination of the long extension wire which connects the leads to the neuro-stimulator wire from the skull area to the chest area in the conventional devices. One of the most frequent failures is due to the breakage of this wire. This was carefully solved by omitting this wire and carefully connecting the electrodes to the DBS system via a short wire in the skull area itself. The possibility of the wire being damaged is significantly reduced.
- Increasing battery efficiency – The battery to be installed into the devices is recharged through an external charger which transmits power by means of a coupled coil system which then feeds an on-chip AC-DC converter. The external charger can be energized without being mounted on the ear, and then worn once fully charged. Once charged the external system can be removed, improving aesthetics and safety. The internal battery would then feed the internal devices.
- Less drug intake – since the drug will be delivered in the local neighbouring affected zones, the drug content can be less. When implanting the DBS device, a single surgical intervention is needed. This includes both the pulse generator and DDS in a single device. Having these two systems incorporated in a single system makes it less stressful and painful for the patient, while giving the patient the benefit of having two implanted systems.
- Throughout the design and planning, it was made sure that the stakeholders' requirements were met. The project initially focused on the miniaturization of the device and finding the ways and the means of improving battery longevity. From the market

research it was highlighted that especially for older adults, the ability to remain independent depends on the ability to manage a complicated medication regime. The idea of designing a DBS system incorporated with a DDS not only results in having an integrated design through a single intervention, but also proves that the patient could be independent. The advantages of advanced drug delivery systems over traditional systems are the ability to deliver a drug more selectively to a specific site, in a more accurate way, with less frequent dosage, decreased variability in the systemic drug concentrations, absorption that is more consistent with the site and mechanism of action, and reductions in toxic metabolites.

- The new DBS system could be custom made to suit the patient's needs, and equipped with selected drugs systems. Further studies can be carried out to explore other possible drug delivery solutions. On the other hand, the DBS does not cater for all the symptoms of Parkinson's disease. While the patient will gradually reduce the drug content, the medication will not be stopped completely. For this reason, the DDS was incorporated within the DBS design in order to cater for the daily drug intake. In addition, if either of the systems fails, since the pulse generator and DDS are combined in a single device the whole device needs to be removed and re-implanted. These two systems cannot be managed separately. The major challenge for the production and manufacturing perspective is to outline the production layout of the DBS device which has the integrated DDS.

6.3 Validity of the Research Results

In order to ensure that the obtained results were reliable and realistic it was important to involve as many respondents as possible. Despite the efforts made, the number of stakeholders who contributed to the study was relatively limited. This was mainly due to the sensitive nature of the project. Also, local expertise in this area is quite limited. On the other hand, the involvement of the main team of professionals coming from different sectors gave an added value throughout the course of the research. The fact that the patients, who have undergone the DBS surgery, were involved, contributed to a broad and detailed evaluation. This was heavily supported by the opportunity to meet a limited number of neurosurgeons, whose contribution proved to be highly beneficial. Further discussions with the sales and production representatives, including both local and foreign organisations would have made the analysis more reliable. The core team was relatively limited to a small sample of professionals. In future research, it would be a good potential input to consider increasing the amount

of team members coming from the different IPD pillars and the quality sector. This ensures that the degree of completeness of the model is also validated.

In addition, the research presented in this paper was focused primarily on the application of the proposed IPD model on a case study of an integrated DBS-DDS system from an engineering perspective. Having said that, to test further the validity of the integrated BioMEMS system from a medical perspective, clinical tests are required. For instance, the type of drug (e.g. GABA or L-DOPA) to be delivered and the location of delivery with respect to the electrical stimulation must be investigated. This shall shed light on the medical feasibility of having a system, which is able to deliver both medication and electrical stimuli.

7 Conclusion

BioMEMS technology deals with the integration of diverse micro-technologies in complex and highly integrated systems. Thus, BioMEMS require special attention with respect to their product development and the wide range of manufacturing technologies which are constantly being developed and updated. The current state and the requirements of BioMEMS technology, collectively led to the need of a methodology, specifically designed and adopted for it.

In conclusion, the key contribution of this paper lies in the proposed IPD model aimed at developing BioMEMS while taking a case study of an integrated DBS-DDS system as an application. Compared to the state-of-the-art, the proposed integrated system provides a number of remarkable benefits. Nevertheless, this is an on-going process which requires further work in order to validate the developed IPD model and to assess the effectiveness of the proposed device solution in a practical scenario.

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