

## Evaluating a Miniature Multisensor Biosignal Recorder for Unsupervised Parkinson's Disease Monitoring

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**Abstract:** An improved miniature biosignal data sensor and recorder device is described, (NAT-1-4G) with 3-axis accelerometer, and a 500 Sa/sec all-channel recording capacity of 36 hours or more with a single zinc-air battery cell, and up to 6 days at 100 Sa/Sec for accelerometer only. Like the previous NAT-1 prototype device, this measures less than 18×22×10 mm and weighs less than 2.3 grams, including the battery. In this paper we describe the device in detail, and introduce the presentation of tremor data measurement captured in the context of Parkinson's disease fore-arm monitoring. The NAT-1-4G device itself has already achieved translation to commercialization and is currently available. *Copyright © 2015 IFSA Publishing, S. L.*

**Keywords:** Neurophysiology, Bio-signal sensors, Medical sensors, Parkinson's Disease.

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### 1. Introduction

It is well understood that use of biosignal data acquisition is increasingly important in many application scenarios, not the least of which are biomedical applications. Often, such measurements are taken in wired or wireless umbilical modes, in other words, within a clinical evaluation setting, with data captured and analyzed over relatively short time windows, and in unnatural settings.

However, the ability to perform ambulatory monitoring of patients provides the possibility of long-duration data capture of bio-parameters in a normal living situation or work-place. This has been an aim for many decades, and has developed from early magnetic tape based data capture [1], to digital systems [2], custom integrated circuits [3-4] and more advanced medical data recorders [5-6]. Such capabilities are identified by many clinical

researchers as being desirable. The opportunity to learn more about medical conditions as well as the condition of individual patients themselves is seen as a major motivator for developing suitable devices. This is very true of applications in the domain of Parkinson's Disease and similar tremor-related medical conditions, where often the primary mode of data capture is limited to a supervised scenario [7-9]. The importance of gathering continuous data for drug management, establishing and gauging long-term prognosis, and the personal reassurance for patients afforded by suitably presented feedback from monitoring systems, can't be underestimated.

The "NAT" (Neural Activity Tracker) project aims to produce a multi-purpose data sensing and recording solution that is extremely small, lightweight and having a recording capacity of days to weeks, dependent upon the selection of parameters such as sample frequency. The NAT-1 device [10]

introduced our first solution to this problem in 2013. Since then we have enhanced and improved the design, resulting in NAT version 1-4G. This newer device includes multiple improvements, including the ability to alter the signal sensitivity of individual recording channels to adapt to a given bio-signal type, including ECG/EEG/EMG/EOG (Electroencephalography, Electro-myography, Electro-cardiography, Electro-oculography), and also auxiliary sensor modules (such as temperature for instance). The NAT-1-4G also retains its capability for tri-axial accelerometer data capture, and in an accelerometer-only recording mode allows 400 samples per second for all three axes, with recording times up to 3 days. At 100 Sa/sec, duration is 6 days.

This paper presents the NAT-1-4G in technical detail in Sections 2 and 3, whilst Section 4 documents some initial experimental applications of the device with a Parkinson's Disease tremor collection scenario. Note that the intention of this paper is not clinical: we do not make any clinically definitive claims about the data collected, but will observe and determine the suitability of the device for capturing such data, and for showing characteristics typically symptomatic of a Parkinson's Disease subject.

Section 5 highlights the additional resources developed alongside NAT, including docking station, wrist-mount, and the infra-red data signature timestamp add-on board. A brief state-of-the-art is given in Section 6, and conclusions presented in Section 7.

## 2. A Small Form-Factor Data Recorder

The NAT-1 is a device family of only 18×22 mm in size, less than 10 mm in height (when using a zinc-air disposable power cell). It weighs less than 2.3 grams, which means it is attractive in applications where regulatory constraints apply (e.g., use with small animals such as mice and other rodents). It is so light in weight as to be quite unobtrusive as a human-subject wearable body-sensor. This low-weight attribute also means that multiple devices can be worn individually or in small groups where appropriate, without causing encumbrance of the subject's normal movements and behavior. We have verified this in a fashion, with team members wearing the device continuously for up to three days (using a 3D-printed wrist-capsule) with no issues.

A NAT-1 device is shown in the image of Fig. 1, with a ball-point pen of normal size for scale. In the photograph provided in Fig. 1, we can see some interesting features. The major part of the device has a profile of less than 4 mm. Also visible in Fig. 1 is a specially designed battery clip for housing a zinc-air cell (as used in hearing aids). This is the gold-plated metal structure. The use of flatter button cells can be envisaged to make a smaller profile possible, though this has weight implications. We also note the potential for ultra-thin flexible lithium polymer

rechargeable batteries, which have a similar footprint and only 2 mm height profile that would align well with the NAT PCB module in situ.

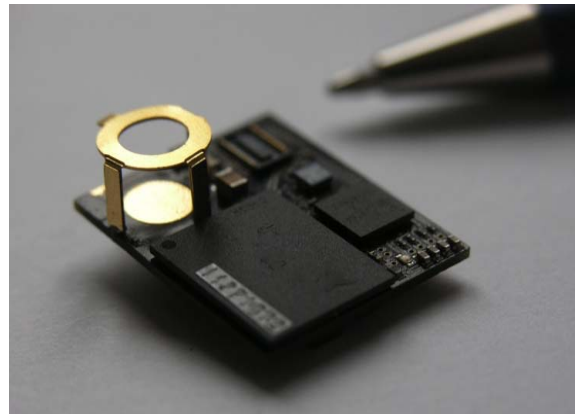


Fig. 1. Top View of NAT-1 Device.

Near the tip of the ball-point pen, one can see a small low-profile connector socket, which is actually a mezzanine daughterboard connector port. This permits a range of possible extension modules. Fig. 2 shows the system level block diagram. As for our previous NAT-1 device [10], this device comprises of three key components – a flash memory chip (largest chip in Fig. 1), a proprietary CPU (mid-sized chip of Fig. 1), and a proprietary MEMS (Micro-Electro-Mechanical System) device for accelerometer (smallest chip of Fig. 1).

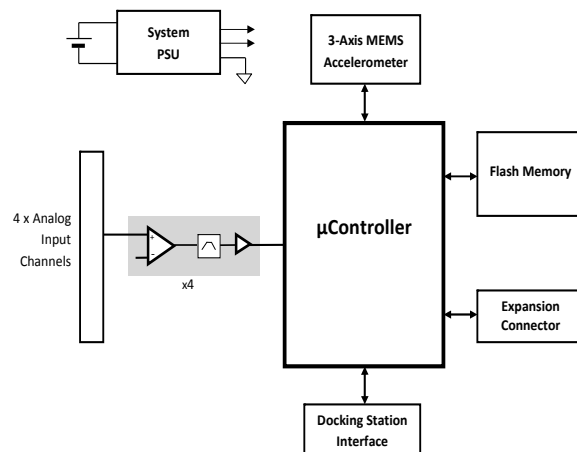


Fig. 2. NAT Device – Sub-component Block Diagram

Additional analogue front-end components provide appropriate signal conditioning for the signal ranges typically encountered in a range of biosensor and biomedical applications. This is augmented by the introduction of programmable gain on a per-channel basis, with signal range up to  $\pm 4$  mV, and ability to scale to signals in the sub-1mV range without appreciable noise.

### 3. NAT-1-4G Device Specification

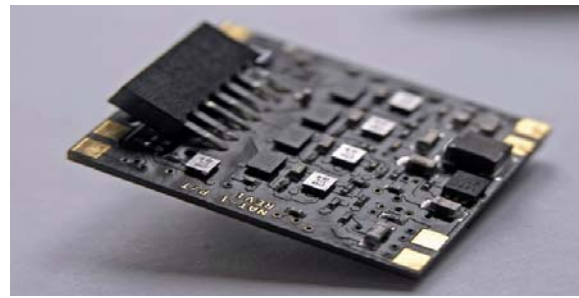
The NAT-1-4G has the specifications as outlined in Table 1.

**Table 1.** NAT-1-4G Specifications.

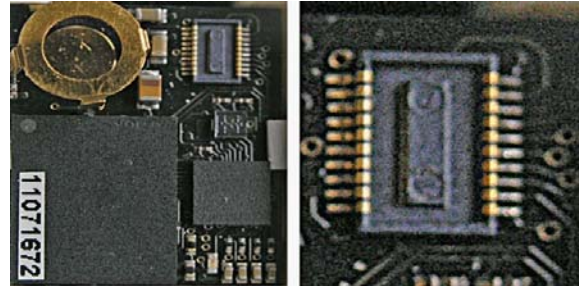
Parameter	Limits	Units
Analogue inputs	4	channels
Bits per analogue channel when used	11	bits
MEMS Accelerometer	3	Axis
Bits per Accel. Axis	8	bits
Sample rate (max)	2000	x 4 ch
Max Current 2 kSa/sec	4.8	mA
500 Sa/sec	2.4	mA
Data Capacity	4 or 8	Gbits
All-Channel Recording Time at 2 kSa/sec	9 or 218 <sup>a</sup>	Hours
Analogue Range	$\pm 1000$ min $\pm 4000$ max	uV
(previous NAT)	$\pm 1000$ <sup>b</sup>	
Accelerometer range	Selectable 2 / 8	G (G-force)
Accelerometer sensitivity	18 / 72	mG (G-force)
<sup>a</sup> Recording time for all channels. Revised device has accelerometer-only option with 6 day record time at 100 Sa/sec.		
<sup>b</sup> Original NAT had fixed $\pm 1$ mV voltage range. Revised NAT range is channel programmable up to $\pm 4$ mV.		

The device has a wide range of possible sample rates, ranging from 100 Sa/sec to 2000 Sa/sec via the user interface software application. At 2000 Sa/sec, the device consumes 4.8 mA of current from a single 1.4-Volt cell, and can record for over 9 hours. An 8-Gbit flash option is possible (NAT-1-8G) and would have over 12 Hours of recording capacity at maximum rates. However, such high sample rates are not necessary for most bio-signal applications we envisage in general long duration monitoring scenarios. At lower sample rates, the capacity of the flash is extended to many days, for example 6 days at 100 Sa/sec for accelerometer only. This compares well with reported state of the art examples [3-4], given that the system is comprised of readily available commodity integrated circuits. The device has three important connection mechanisms, these being the analog input connector (angled connector block to left of device in Fig. 3a), the daughterboard extension socket (Fig. 3b) and the docking-shoe corner pads (seen in Fig. 3a)

A particular feature of NAT-1 was the use of a single zinc-air power cell. Such cells are widely used in hearing aids, and have an active power-delivery life-span of around two weeks, after which the cell begins to cease to be viable. We have retained this mode of power provision in NAT-1-4G. However the possibility of using alternative power cells is being actively investigated at present. To date, the Zinc-Air modules offer the best power density for size and weight with considerable record times up to 2 weeks.



(a)



(b)

**Fig. 3.** (a) Analogue Connector Port on NAT-1 Device Underside, and (b) Overhead View of NAT and Daughterboard Connector.

### 4. Evaluation Methodology

Previously, most of the testing of the device has been limited to test scenarios including (a) EEG and Accelerometer data collection from mice in live test scenarios undertaken by researchers at the University of Aberdeen, (b) a preliminary EMG capture evaluation at the University of York, and a (c) high-G test setting using a golf-club attachment to capture golf swing behaviors in terms of club rotation, side-movement and swing-path motion [10]. In all cases, the device was used untethered and powered exclusively with a single zinc-air cell. This work was aimed at gaining an initial scope of capabilities of the device. In this paper, with the newer NAT-1-4G, we describe the use of the device in capturing tremor motion in a Parkinson's disease subject, and we compare this to data captured in the same way for healthy control subjects. This is a limited test-scenario owing more to engineering evaluation than clinical study, and should not be considered as a practical clinical evaluation study.

The experimental method consisted of a wrist-mounted device (see later Section 6 for details and photographs) which in most cases is worn continuously for several days, and only being removed where not appropriate for the device operation (e.g. whilst showering). All three accelerometer channels were sampled at 500 Sa/sec with a resolution of 8 bits per channel for a full-scale range of  $\pm 2000$  milli-G. An important aspect of the data collection is that there is no knowledge of activities during data collection (it is unsupervised).

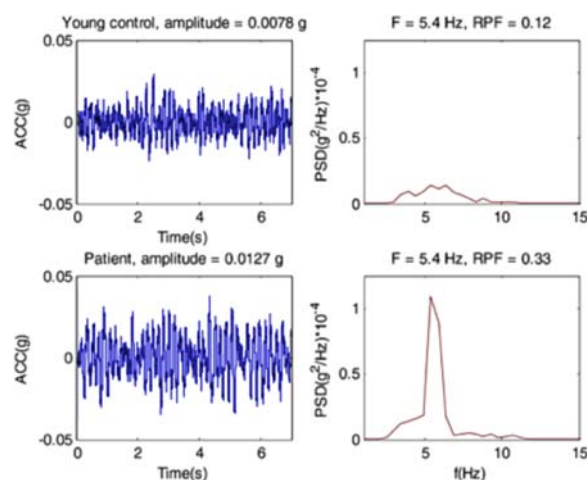
Unlike short laboratory assessed (supervised) tremor measurements, where a series of directed or constrained actions are monitored for a period of perhaps 1 hour, here the data was collected blindly for up to 72 hours. This presents particular issues for data interpretation which we discuss further in later sections. The purpose of the evaluation was to make a straightforward determination that the NAT-1-4G device is (or is not) capable of gathering potentially clinically-useful tremor data during long unsupervised periods of use.

In order to understand our evaluation, it is useful to first of all exemplify the typical data characteristics likely to be observed in such an experimental study. A common aspect of Parkinson's tremor is the presentation of an excess of frequency components in the 5 to 7 Hz range as compared to typical healthy subjects.

The example of Fig. 4, reproduced from a recent publication [11], illustrates this quite well. It is seen that a control subject has a relatively broad range of frequency components in movement measurements, whilst a Parkinson's patient exhibits a classical dominant frequency peak centered around the 5-6 Hz frequency, (often described as the unilateral or bilateral resting tremor) which is attributed to motor-neuron induced involuntary movements in the instrumented limb. These components usually have noticeably larger magnitudes than typical average motions generated by intended limb motion.

It is important perhaps to note that there is a significant difference between a resting limb exhibiting tremor (as might be observed under a controlled measurement scenario) and a limb measured over a significant timescale with unsupervised 'every-day' behaviors. The challenge

for long-term unsupervised monitoring is to distill reliable indicators from inherently component-rich data sets. NAT-1-4G can of course be used for both a controlled resting limb study and an unsupervised data recording scenario.



**Fig. 4.** Example of Parkinson's Tremor components centered around 5 to 6 Hz for control (top) and affected patient (bottom). Reproduced from Meigal, *et al.* [11].

In terms of existing devices, of which there are too many to present a comprehensive survey here, we have surveyed a subset of current devices that have succeeded in achieving commercial translation into common use, as tabulated in Table 2, for comparative purposes. Several of these are wirelessly tethered devices via radio link, and several are non-wireless devices, including NAT-1-4G itself.

**Table 2.** Comparison With Some Recently Reported Devices.

Device & Type	SIZE & WEIGHT	Battery Type & Record Time	Sensors and Inputs	Sample Rates	Data Storage	Refs if any
<b>MCRROBERTS HYBRID</b> Bluetooth Tethered	87×45×17 mm 74 grams	Lithium Polymer 60 hrs at 100 Hz	2G tri-axial accelerometer triaxial Gyroscope	100 Sa/sec	SD card	[16]
<b>Neurologger 2A</b> Untethered EEG logger	22×15×5 mm 1.7 grams with battery and 3-axis accelerometer	2x ZN10 battery 124 hrs at 100 Hz 32 hrs at 400 Hz	4 channel analog input extra board provides triaxial accelerometer with additional weight (about 0.4 gram)	100 Sa/sec up to 19 kSa/sec for one channel 1000 Hz for accelerometer	On board flash Up to 1 GBit	[17]
<b>G-Link</b> Wireless tethered	58×43×21 mm 40 grams	Lithium polymer Record time not stated	2 G/10 G Triaxial accelerometer, temperature sensor	2 channel (accel/temp) 4 kSa/sec 4 channel 2 kSa/sec	Onboard 2 Mbyte	[18]
<b>NAT-4G</b> Untethered EEG/EMG/ECG and Accel Logger	22×18×10 mm < 2.3 grams with battery	Zinc-Air hearing aid battery 9 hours at 2000 Sa/sec 72 hours at 250 Sa/sec >6 days at 100 Sa/sec	2 G/8 G triaxial Accelerometer 4 channel ±4 mV analog in	Up to 2000 Sa/sec	Built in Flash 4 or 8 Gbit	This paper

The Neurologger-2A device has some similar sets of capabilities to the NAT-1-4G, as might be expected as it is a similar onboard storage recorder, whereas the wireless devices have significant demands for power, requiring larger batteries and more circuitry. It can be seen that NAT-1-4G provides the smallest, lightest, and longest recording lengths for a device integrating both accelerometer and analogue sensor (e.g. EEG) channel recording as standard. Neurologger-2 with add-on accelerometer board has comparable weight and size to NAT-1-4G. The NAT-1-4G device has a large signal range and is programmable to accept analogue signal inputs up to  $\pm 4$  mV and can be reduced to  $\pm 1000 \mu\text{V}$  for high-sensitivity.

Ambulatory monitoring has importance for the role of extended out-patient monitoring of EEG as a diagnostic aid and guide to treatment [12-13]. Recent work in this field includes many wireless approaches to ambulatory monitoring, but these are effectively 'tethered' via a secondary monitoring or recording station [14-15]. Recent literature reports an 8-channel EEG sensor node which "measures 35 mm $\times$ 30 mm $\times$ 5 mm excluding Li-ion battery" [14], and power consumption in the range of 27-42 mW, equivalent to around 3 to 5 mW per channel.

## 5. Evaluation and Results

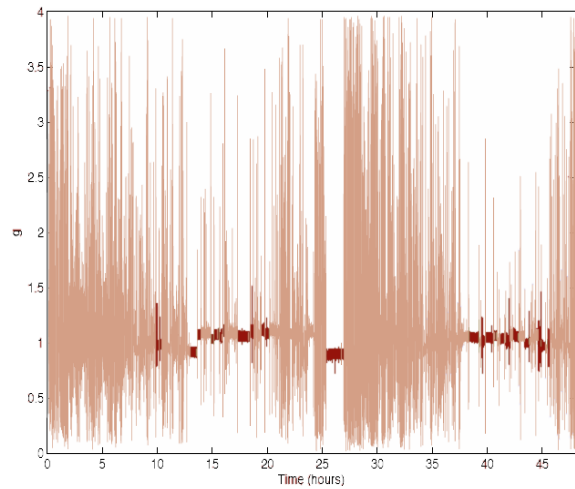
After gathering data from a small study of four subjects, various data processing approaches were explored to derive useful data. The initial raw data sets contain a number of artifacts that need to be managed. Inevitably the accelerometer range encounters clipping (saturation), since the sensitivity of the accelerometer scale needs to be fine enough to detect tremor motions, even though other motions in unsupervised data collection can be more dynamic. A second issue is that of constant-G offsets caused by orientations of the limb, in this case the wrist, and in different postures for instance. Both of these aspects may be observed in Fig. 5a, which shows the raw data collected over a 48-hour period, and clearly exhibits variable constant-G offsets as well as saturation.

Fig. 5a highlights a further aspect of interest, colored in red on the trace. In the data survey we have conducted we have observed that it is possible to automate identification of 'quiet periods' where activity is relatively low. These are analogous to a resting limb, though in fact these so-called quiet periods contain non-resting activity, but less so than other segments of the data. The algorithmic approach to identification of quiet periods is described as follows:

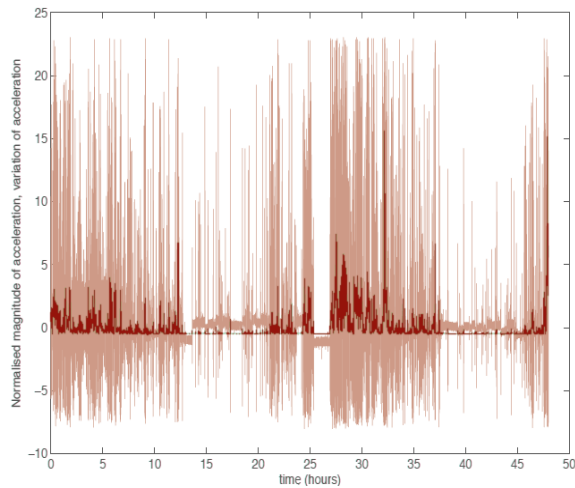
We define *noisiness* with respect to a signal as defined in Equation 1, for case of the parameter  $k_0$  to be as stated in Equation 2.

$$\{f_k\}_{k \in \{1,2,3,\dots,N\}} \quad (1)$$

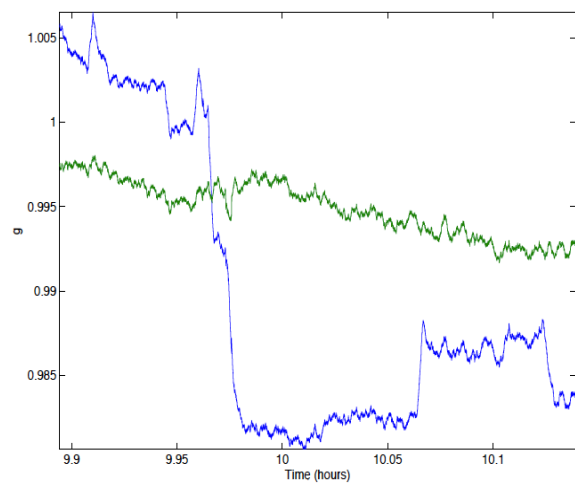
$$v_{k_0} = \sum_{l=k_0-s+1}^{k_0+s} |f_l - f_{l-1}| \quad (2)$$



**Fig. 5a.** Raw Data Collection over 48 hours (where red sections represent 'quiet' periods).



**Fig. 5b.** Raw data and Magnitude after Constant-G Correction (where red represents adjusted data).



**Fig. 5c.** Magnitude of Acceleration with Correction (blue - original data, green - offsets removed).

For Equation 2, the constant  $s$  is chosen such that the time distance between the occurrence of  $f_{k_0-s}$  and that of  $f_{k_0+s}$  is as close as possible to 1 s. We note that  $v_{k_0}$  is defined only for:

$$k_0 = s+1, s+2, \dots, N-s$$

To segment a signal into noisy and quiet *periods*, we threshold  $v_k$  by  $\theta$  and say that a noisy *moment*  $k$  is given by ( $v_k \geq \theta$ ) and a quiet one by ( $v_k < \theta$ ).

A *quiet* period is then given by 2 s or more consecutive quiet moments, and noisy periods consist of the moments outside quiet periods.

In general, we adapt the threshold to the trace by setting  $\theta = \mu_v - 0.3\sigma_v$ , where  $\mu_v$  and  $\sigma_v$  are the mean and standard deviation of  $v_k$  over its defined values. This is done to take account of the possibly varying baseline activity between subjects, and between their hands. The value 0.3 used here is an empirically selected value, which appears to make a good job of segmentation.

Meanwhile, by applying very-low-frequency component extraction and adjustments to the raw data, it is possible to remove the earlier mentioned constant-G offsets from the data, whereupon it is possible to plot the magnitude of acceleration of the data on each channel without bias due to such offsets. This is illustrated by Fig. 5b, which shows the normalized magnitude in red against the whole data set in pink. Fig. 5c shows a small segment of the data with the raw data magnitude plot versus the offset adjusted case.

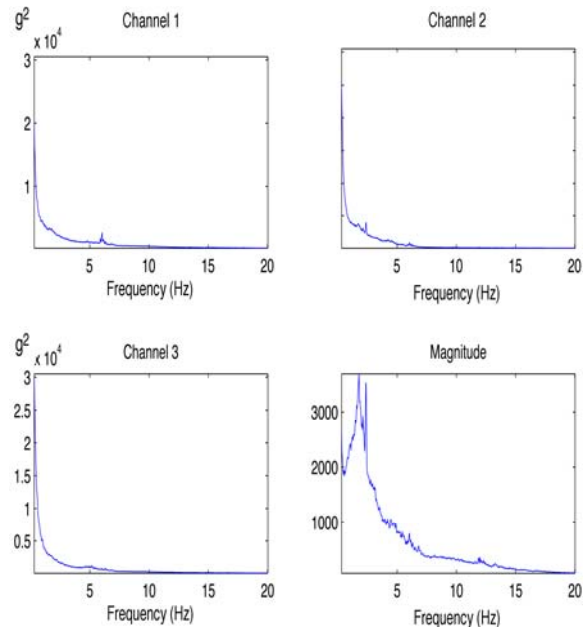
Once these treatments are applied to the gathered data, it becomes possible to generate power-spectra plots of magnitude versus frequency components using FFT analysis. We may then plot each accelerometer axis as well as a combined power spectra plot, which combines motion from all three axes. Fig. 6a shows such a collection of plots for a healthy subject, whilst Fig. 6b shows the same for a known Parkinson's disease volunteer. It is already noticeable that the Parkinson's disease plots show the classical excess of activity in the 5 to 6 Hz region.

Fig. 7a and Fig. 7b show the combined data sets for four human volunteers for comparison. The subjects included three healthy individuals and one Parkinson's disease diagnosed subject. Data was collected for each wrist (left/right) on separate occasions. When only the quiet periods of the data sets are analyzed, the components of the data become less 'cluttered'. That is not to say there is not much to be discovered by analyzing a more complex data context – but rather that there is much to be done to develop useful analytical models from such data sets.

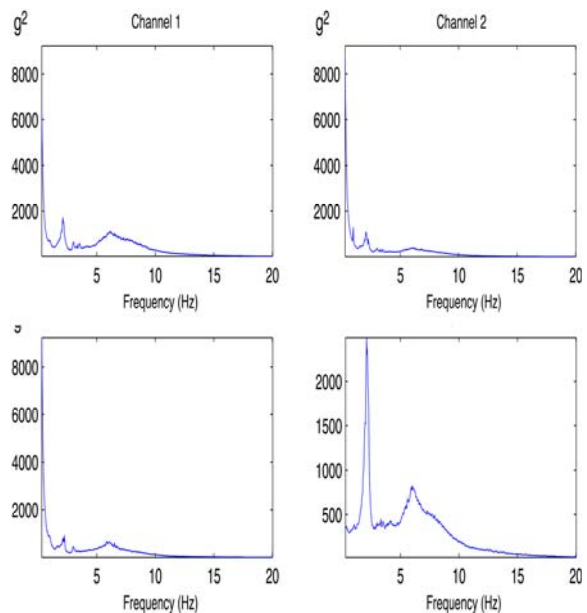
Fig. 8a and Fig. 8b show examples of non-selective data analysis (i.e. all data from a multi-day data capture run) and using the so-called 'quiet periods' only.

In the healthy subjects the plots have a clearly defined roll-off toward 20 Hz and if the slope of the characteristic was subtracted from these plots there would be a fairly uniform response. In the case of the

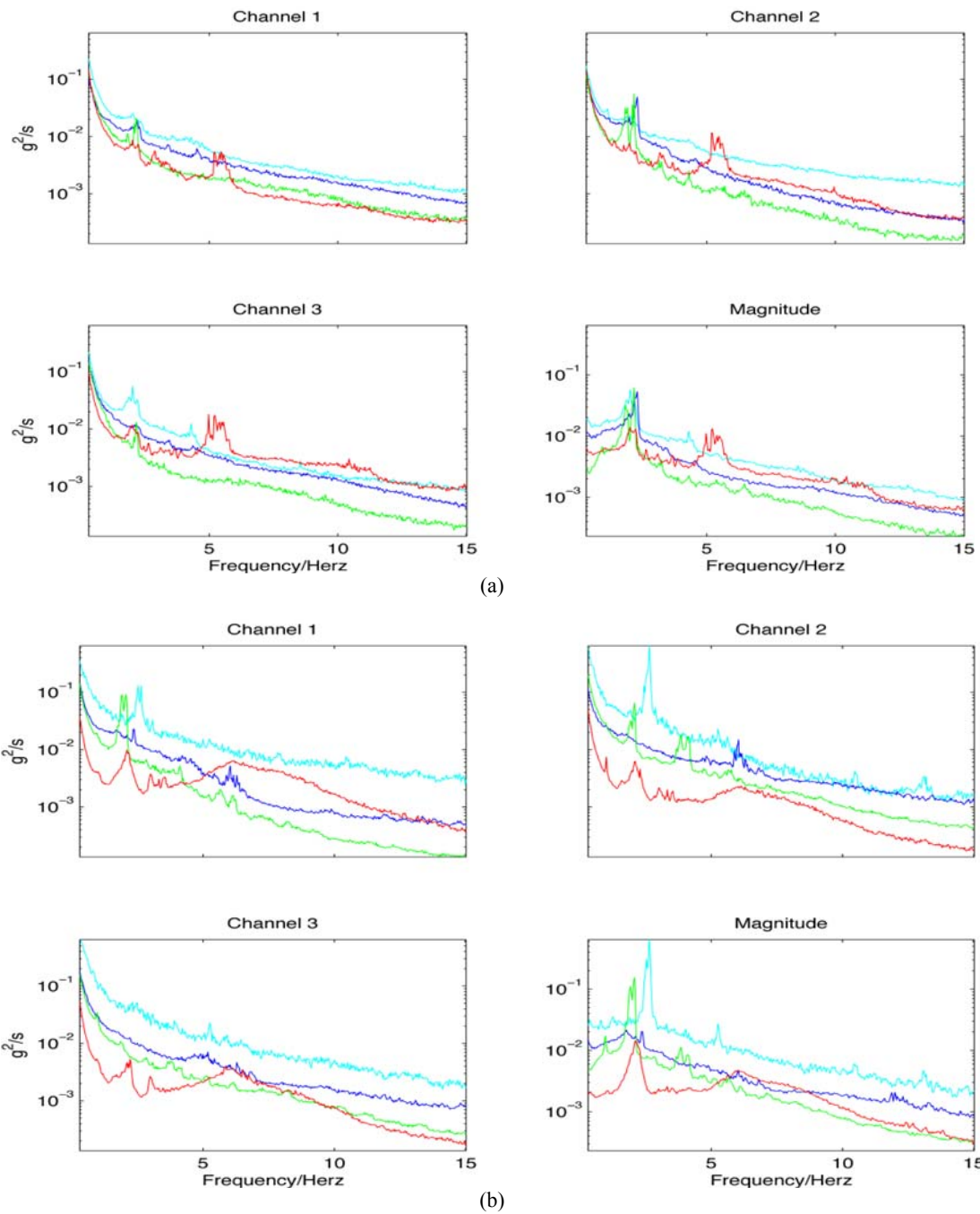
Parkinson's subject however, one can observe an obvious excess of frequency activity in the 5 to 7 Hz range and this correlates well with our expectation if the device were capable of effective collection of tremor data. We note that the left and right hand characteristics of the Parkinson's disease volunteer are different. This may reflect the fact that the dominant limb and non-dominant limb have different use in every-day activity and/or a function of the tremor being non-symmetrically presented.



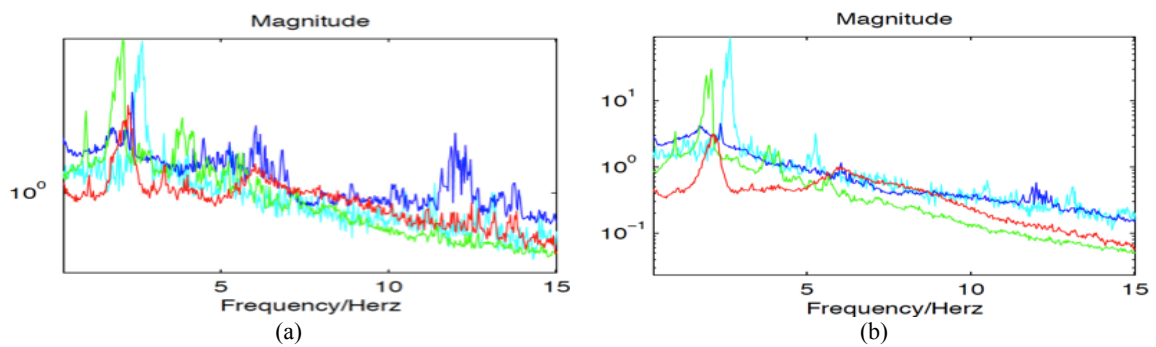
**Fig. 6a.** Three-Axis Power Spectra (Non-Parkinson) (right - dominant - hand), showing channels 1, 2 and 3, plus combined magnitude, linear vertical scale.



**Fig. 6b.** Three-Axis Power Spectra (Parkinson) (right - dominant - hand, showing channels 1, 2 and 3, plus combined magnitude, linear vertical scale).



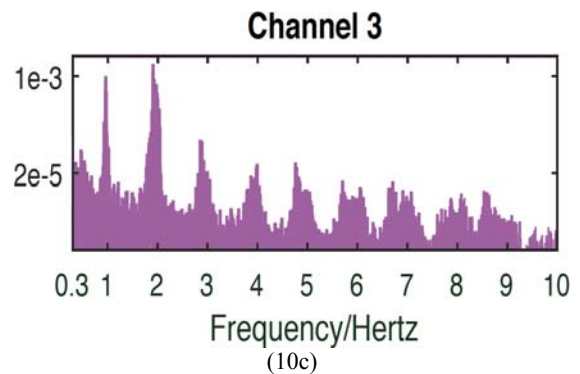
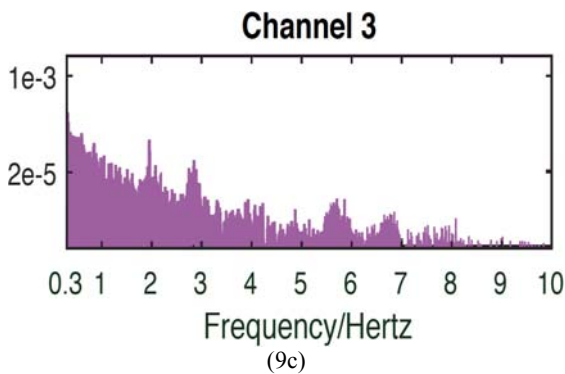
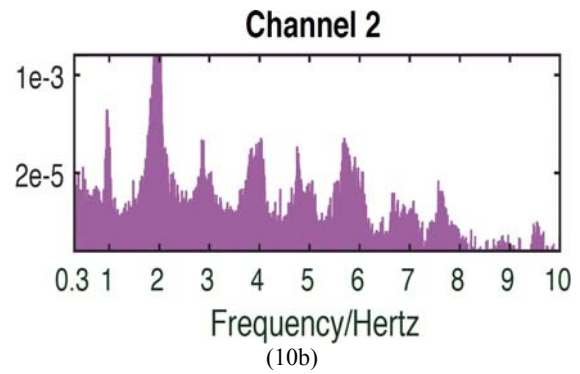
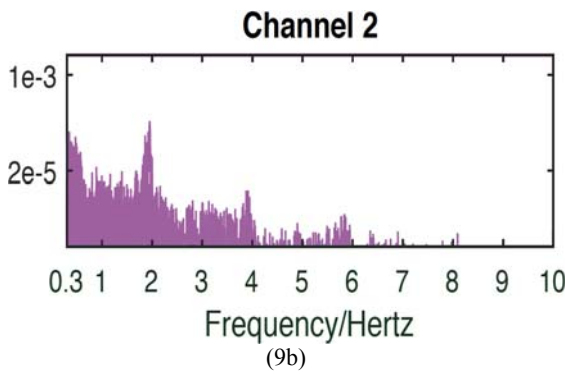
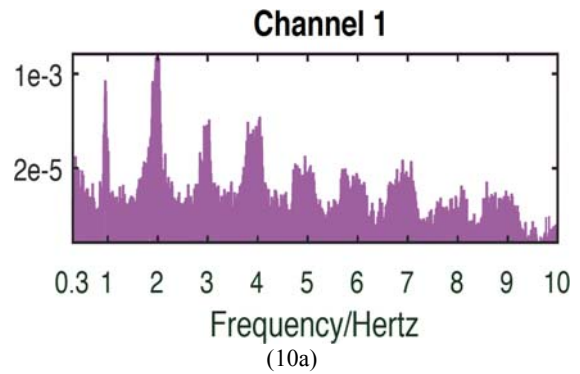
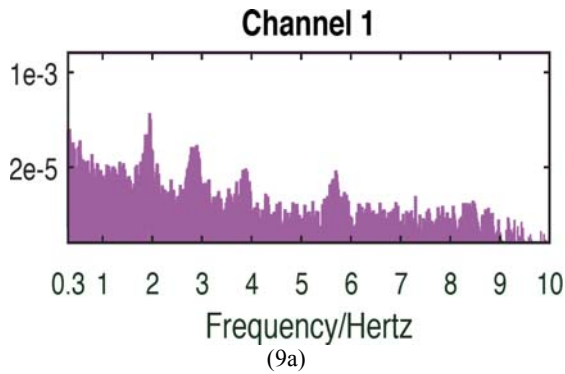
**Fig. 7.** Power Spectra for Parkinson's Case and Controls: (a) Left Wrist, (b) Right Wrist (Parkinson's subject red, blue and green are controls, right wrist Data Collection, log vertical scale).



**Fig. 8.** Frequency vs. Magnitude for All, (a) without selectivity, and (b) with 'quiet period' selectivity (right wrist, trace colours as noted in Fig. 7).

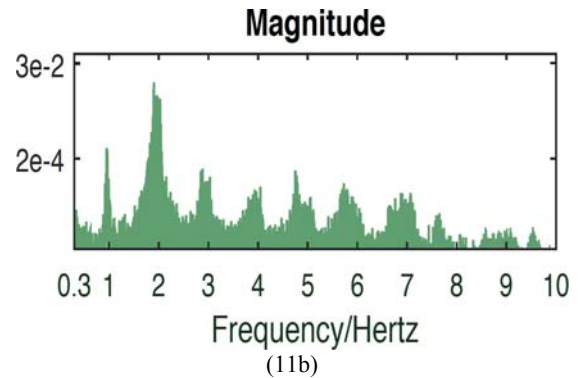
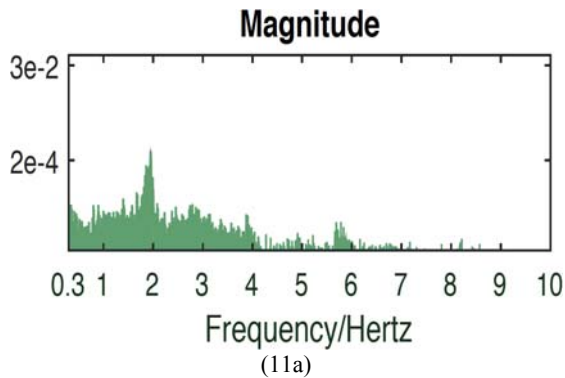
All of the subjects exhibited a strong signal in the area of 1 to 2 Hz, which we attributed to walking and gait behavior in our preliminary

report [19]. We conducted further tests on this aspect, resulting in data reported in Fig. 9, Fig. 10 and Fig. 11.



**Fig. 9.** Accelerometer Channel Frequency Components for Walking with Hands in Pockets.

**Fig. 10.** Accelerometer Channel Frequency Components for Walking with hands free.



**Fig. 11.** Frequency Spectrum of magnitude of change for all Accelerometer channels combined, showing (a) walking with hands in pockets, and (b) walking with hands free.

Fig. 9 shows the tri-axial accelerometer data for a subject walking with hands restricted (hands in pockets). Fig. 10 shows the same data but with hands free to swing in a normal walking mode. Fig. 11 shows the combined data for both cases as a magnitude plot. In all cases the data is presented as a frequency component trend. The main observation here is that walking with hands free there is a peak at around 1 Hz whereas this is missing in the ‘hands in pockets’ case, and the 2 Hz component is substantially reduced. This tends to back up our view that the 1-2 Hz peak in the long duration recordings is due to walking related motion components. This could prove to be very useful.

As noted earlier this is not intended to be a clinical study – rather an observation of the suitability of our device for long term signal capture in this domain – can we capture data that is useful in differentiating tremor related micro-movements? The data captured seems to confirm the value of the device for such work.

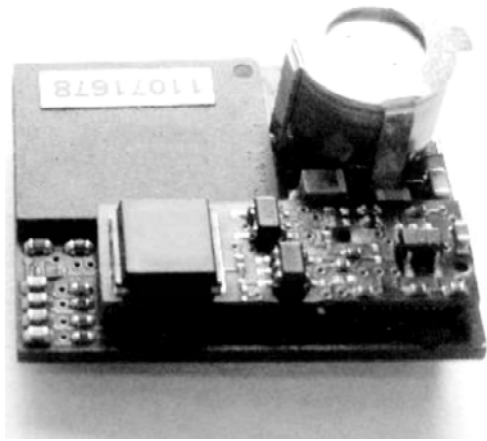
## 6. Docking Station, Analysis Tools and Extension Boards

The NAT device family has the advantage of being provided with a bespoke docking station, for download of recorded data from flash via USB. This is illustrated in Fig. 12. Once downloaded, the data can be processed using Cybula Ltd Signal Data Explorer software suite, which can be trained to perform auto detection and classification of signal behaviors and events [10]. Available add-ons also include an infra-red time-code recording daughterboard which records infrared pulse code streams along-side the analogue channels (see Fig. 13 showing IR device fitted onto the NAT module).

Fig. 14 shows the wrist-mount prototype capsule in various views when worn. The wrist module is quite compact but could be further reduced in size. With certain power cells the format and size of the capsule could certainly be reduced considerably. These early prototype capsules were developed using 3D rapid prototyping (close up view shown in Fig. 15). We are currently working on more sophisticated one-piece wrist-mount modules with integral strap, and using more flexible plastics.



**Fig. 12.** NAT USB docking station.



**Fig. 13.** NAT1-IRDB Infra-red Receiver Daughter-Board, Shown mounted on a NAT device.



**Fig. 14.** NAT Wrist-Mounted Early Prototype Capsule.



**Fig. 15.** Close-up of NAT Capsule Prototype.

Future developments for the daughterboard connector socket could include RF telemetry functions and a micro-backplane to permit multiple NAT devices to be ganged and synchronized to perform something like 16 or 32 channel acquisition, thus linking multiple NATs in a synchronized data capture mode. This is particularly interesting for multi-limb monitoring where relationships between respective limb data-sets might be of interest.

## 7. Conclusions and Future Work

The improvements made to the NAT-1-4G device are undoubtedly beneficial for its wider use in application areas such as EEG, EMG and in more complex mixed monitoring scenarios. This includes combined tremor-motion and EMG capture in patients with conditions such as Parkinson's disease: a key area of interest at the present time. Research continues within our group on more sophisticated data analysis and algorithmic treatment of gathered data in long-duration unsupervised contexts. The use of low sample rates for accelerometer data recording of the order of 7 days is possible with the newer device, and we hope in future to evaluate the tradeoff between data quality and sample rates to establish a clinically useful long-duration recording configuration. The York team [20] and partners CYBULA Ltd. [21] are very interested in developing collaborative partnerships and would welcome enquiries from prospective evaluators and end-users in the clinical domain at the present time.

This work forms the first phase of a longer-term research project in which we expect to continue to collect data in increasingly sophisticated scenarios with continuous data capture over months and possibly years. The particular aim is to achieve clinically useful continuous unsupervised and untethered monitoring in every-day environments.

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