A NON-INVASIVE SYSTEM FOR REAL-TIME DETECTION AND TREATMENT OF SLEEP APNEA EPISODES

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This thesis is the result of the author's original research. It has been composed by the author and has not been previously submitted for examination which has led to the award of a degree.

Signed: *Date:*

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Abstract

A Non-Invasive System for Real-Time Detection and Treatment of Sleep Apnea Episodes

Sleep apnea is a sleep disorder affecting approximately 3% of the UK population. During sleep, a person's airway becomes blocked, causing them to waken many times per hour to restore their breathing. This can result in excessive daytime tiredness, cardiac problems and other health issues. Diagnosis of sleep apnea is currently performed using polysomnography, where multiple physiological parameters are measured overnight in a sleep laboratory. However, polysomnography is expensive and uncomfortable. The most successful current method of treating sleep apnea is continuous positive airway pressure (CPAP), involving nightly wearing of a pressurised mask to keep the airway open. CPAP is not successful for all patients. There is a need for new methods of detection and treatment of sleep apnea.

This thesis provides a review of current methods of diagnosis of sleep apnea, discussing their benefits and problems with a view to real-time monitoring. The use of a pressure sensitive mat to detect breathing is then discussed, including a review of products currently on the market. A summary of current sleep apnea treatment methods is then provided. This is followed by a review of possible methods of interrupting individual sleep apnea episodes to restore breathing.

The development of a new practical device for sleep apnea detection and treatment is then discussed. The device uses a pressure sensitive mat located under the patient's mattress to monitor breathing movements in real time. Absence of a breathing signal triggers a vibrating device to induce the patient to move and resume breathing without awakening. Initial testing on the viability of such a device is described. In conclusion, for some sleep apnea patients, this type of device may provide a useful alternative to the currently available treatment methods.

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1. Introduction

Sleep apnea (alternatively spelled as 'apnoea') is a sleep disorder affecting at least about 3% of the population (Young et al, 1993). A large number of further cases appear to be undiagnosed and untreated (Young et al, 1997). During sleep, many times per hour, a person's airway becomes blocked or their respiratory drive stops operating correctly. This causes them to stop breathing and to awaken, potentially hundreds of times per night, in order to restore their breathing. The lack of quality sleep, together with physiological effects from constant drops in blood oxygen levels, can result in serious short term and long term health issues. Diagnosis of sleep apnea has traditionally been performed by overnight recording of multiple physiological parameters in a sleep laboratory, which is a lengthy and expensive procedure. Current treatment options include the nightly wearing of a pressurised mask to provide continuous positive airway pressure (CPAP), lifestyle changes or surgery, but none of these are completely satisfactory. There is a need for a device to detect sleep apnea in real-time, but also to interrupt and stop the sleep apnea episode so that normal breathing can be restored without wakening the patient.

This thesis firstly provides a review of current methods of diagnosis of sleep apnea. The different types of physiological signal that have been used for detection are considered, including respiratory air flow, blood oxygen levels, heart rate variability (HRV), respiratory effort and electromyogram (EMG). The suitability of these different signals for reliable real-time detection and diagnosis in a home environment is discussed. The idea of real-time detection of sleep apnea episodes using a pressure sensitive mat is then discussed, including a review of baby movement monitoring mats that are currently available on the market, which could be adapted for use in sleep apnea monitoring.

A review of current methods of sleep apnea treatment is then provided, with a discussion of why none of these methods are satisfactory for some patients. This is followed by a review of possible methods of interrupting individual sleep apnea episodes.

The development of a new practical device for sleep apnea detection and treatment is then discussed. The device consists of a pressure sensitive mat located under the patient's mattress to monitor their breathing movements in real-time, and a small vibrating motor that is activated to stimulate the patient if their breathing stops, so that they will restart their breathing without wakening, Results of some initial testing on the viability of such a device are presented. Although this type of device may not work well with all sleep apnea patients, it may be very useful for other sleep apnea patients, providing a viable alternative to the currently available treatment methods.

2. General Background on Sleep Apnea and Sleep

Sleep apnea is a type of sleep disordered breathing. In 1999, an American Academy of Sleep Medicine Task Force set out standard diagnostic criteria for sleep apnea syndrome (AASM 1999). They defined a sleep apnea episode as occurring when a person stopped breathing for at least 10 seconds, although often in practice the breathing may cease for up to a minute or longer. In cases where the airway is significantly obstructed but not fully blocked, with at least a 50% reduction in baseline ventilation, the episode is described as hypopnea, rather than apnea. Hypopnea can also be very detrimental to the patient's health if it occurs frequently and repeatedly

The severity of sleep apnea may be defined by the apnea/hypopnea index (AHI), also known as the respiratory disturbance index (RDI), which is defined as the number of breathing cessations per hour. The minimum generally accepted AHI for a sleep apnea diagnosis is 5 cessations per hour (AASM 1999). 5-14 episodes per hour is considered to be mild sleep apnea, 14-30 is considered moderate, and over 30 is considered severe. Prior to the AASM study, many researchers used different criteria to define sleep apnea, for example, setting a higher minimum AHI threshold such as 10 or 15 episodes per hour, and taking into account the severity of other symptoms experienced by the patient.

Risk factors for sleep apnea include being overweight or obese, being over 40 years old, and being male. However, sleep apnea can affect anyone, including children (Kuhle 2009). Smoking and alcohol use (especially near bedtime) are further risk factors. The risk is also increased by anatomical factors such as craniofacial abnormalities, increased tissue mass in the pharynx and nasal obstruction, and a family history of sleep apnea.

Often sleep apnea goes undiagnosed, due to a lack of public awareness of the condition. People with sleep apnea or hypopnea may not actually be aware that they have a sleep disorder and may not remember the many transient arousals that they

have experienced during the night. Frequently, it is the patient's bed partner who first becomes aware that a problem exists.

Healthy people without sleep apnea syndrome will often have irregular breathing as they fall asleep. They may also have brief breathing cessations, particularly as they first fall asleep and during REM sleep. However, normally a healthy person would experience no more than 10-20 apnea episodes in total per night.

2.1 Types of sleep apnea

The most common form of sleep apnea is obstructive sleep apnea (OSA), in which the airway becomes physically blocked during sleep by tissues of the throat region and upper airway. This can include the tonsils, the soft palate, the uvula, the tongue and the lateral pharyngeal walls. At least 20 muscles are involved in active constriction and dilation of the upper airway (Ayappa & Rapoport 2003). These muscles interact in a complex fashion to control the positions of the soft palate, the tongue, the hyoid apparatus and the walls of the pharynx. The muscles relax during sleep and muscle tone decreases, resulting in a narrowing or blockage of the airway with a collapse of the tongue, the soft palate, the uvula or the epiglottis, as shown in figure 1 below. The collapse may occur at a single location, or it may occur simultaneously at multiple locations within the throat region.

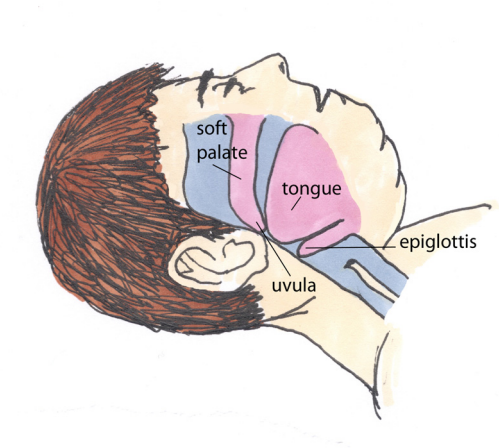


Figure 1: Blockage of the airway during sleep in an OSA patient

In an attempt to resume breathing again, the sleeping person increases their respiratory effort. However, this can actually make the problem worse, because negative pressure differences in the lungs may generate a suction effect on the soft tissue of the throat. Eventually, the lack of breathing causes a transient arousal from sleep, allowing normal muscle tone to be restored and breathing to be restarted. As a result of this occurring many times per hour, the person suffers from extremely poor quality, fragmented sleep. They also suffer from the longer term health problems associated with frequent periods of low blood oxygen and high levels of carbon dioxide.

A less common form of sleep apnea is central sleep apnea (CSA), where there is no physical blockage in the airway, but the neural signalling from the patient's brain to their breathing muscles stops or malfunctions, causing breathing cessation. In some cases, central sleep apnea may develop due to head injuries or diseases of the nervous system. It may also arise as a result of excessive use of respiratory depressant drugs such as heroin or other opiates, which have the effect of damping the activity of the brain's respiratory control centres. An overdose of such drugs may cause death by shutting off the breathing altogether. Patients with heart failure sometimes develop central sleep apnea, and this may disappear again if the heart condition can be successfully treated.

Some patients have a combination of obstructive and central sleep apnea, and this is known as mixed apnea. A mixed apnea episode tends to start as central sleep apnea and then develop an obstructive apnea component. In patients with severe long term obstructive sleep apnea, the loss of the central respiratory drive sometimes also develops, so that the patient develops central sleep apnea as well. It is thought that this is due to acid-base and carbon dioxide feedback malfunctions that arise due to heart failure.

Figure 2 below, from van Houwelingen (1999), shows a comparison of the airflow, abdominal effort, thoracic effort and blood oxygen saturation over a period of time for episodes of central sleep apnea, obstructive sleep apnea and mixed sleep apnea.

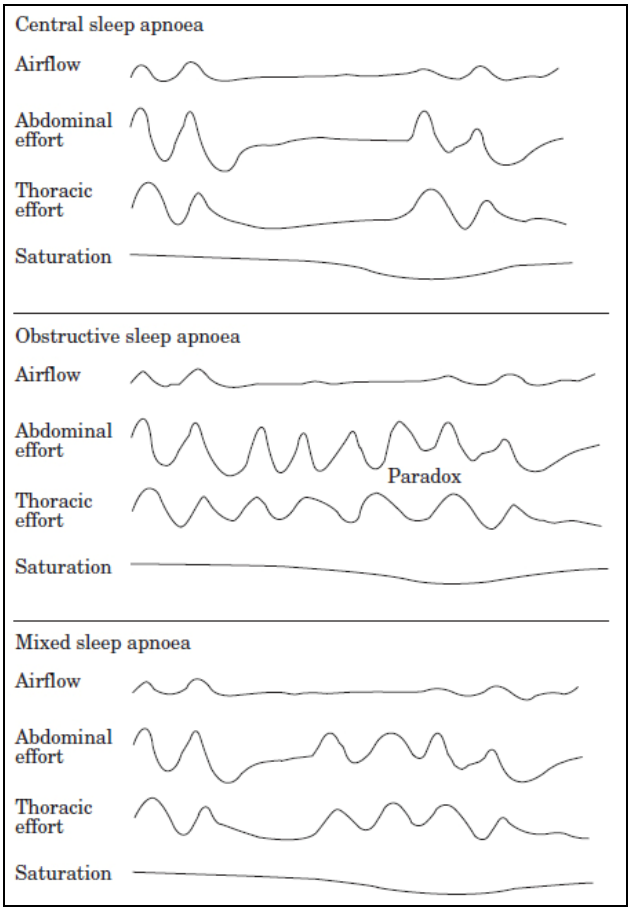


Figure 2: Comparison of CSA, OSA and mixed sleep apnea (van Houwelingen 1999)

As can be seen from figure 2, the airflow and oxygen saturation drop in all three cases. However, although the abdominal and thoracic effort stops in central and mixed sleep apnea, it actually continues during obstructive sleep apnea (OSA) as the patient attempts to breath, and will generally increase as the sleep apnea episode progresses. The respiratory efforts of the chest and abdomen will frequently be out of phase during an OSA episode. Mixed sleep apnea starts like central sleep apnea, but then changes to look more like obstructive sleep apnea.

2.2 The need for sleep

One of the main problems with untreated sleep apnea is the consistent lack of quality sleep. The function of sleep is not well understood, but it is known that sleep is essential to life. Under conditions of complete sleep deprivation, death occurs within

a few weeks (Dement 2000). Sleep is characterised by motor rest, increased sensory thresholds, easy reversibility (unlike a coma state), stereotyped posture, the use of specific rest sites (e.g. a bed), circadian organisation, sleep regulation (e.g. affecting hormone balance) and closed eyes (Nicolau et al, 2000). One popular theory is that sleep exists to allow metabolic restoration in the brain and remodelling of synaptic function (Douglas, 2002). Insufficient sleep can cause numerous problems, including excess daytime tiredness, fatigue, lack of concentration, low reaction times, vision problems, impaired cognition, reduced memory function and impaired judgement, and some or all of these can be observed in untreated sleep apnea patients. As a result, the person may experience severe difficulties in many occupations and the probability of accidents is greatly increased, e.g. while machine operating and driving a vehicle. Other adverse effects may include low motivation, moodiness, depression or aggressiveness, with negative effects in both work and social situations. Sleep disorders, such as sleep apnea, are thus very serious matters, which have historically received far less attention than is deserved.

Sleep has several distinct stages, which can be identified using an electroencephalogram (EEG) machine. Different brain wave frequencies and characteristic patterns are seen in each of the different sleep stages, as shown in figure 3. The two main categories of sleep are REM (rapid eye movement) sleep and non-REM sleep (also known as NREM). NREM sleep includes stages 1, 2, 3 and 4, where stage 1 is light sleep, and the depth of sleep increases with stages 2, 3 and 4, stage 4 being the deepest stage of sleep. In stage 1 sleep, EEG frequencies of approximately 4-7 Hz are observed, and these are known as theta wave frequencies. This is in contrast to the beta wave frequencies of 14-25 Hz seen during normal wakefulness, and the alpha wave frequencies of approximately 8-13 Hz observed during relaxation. In Stage 2 sleep, theta waves are again seen, but characteristic patterns known as spindles and K-complexes can also be observed. In stage 3 sleep, delta frequencies of approximately 2 Hz or less are observed for some of the time. In stage 4 sleep, the entire EEG signal shows delta frequencies. During NREM sleep, the parasympathetic nervous system is dominant, but during wakefulness, the sympathetic nervous system tends to be more active.

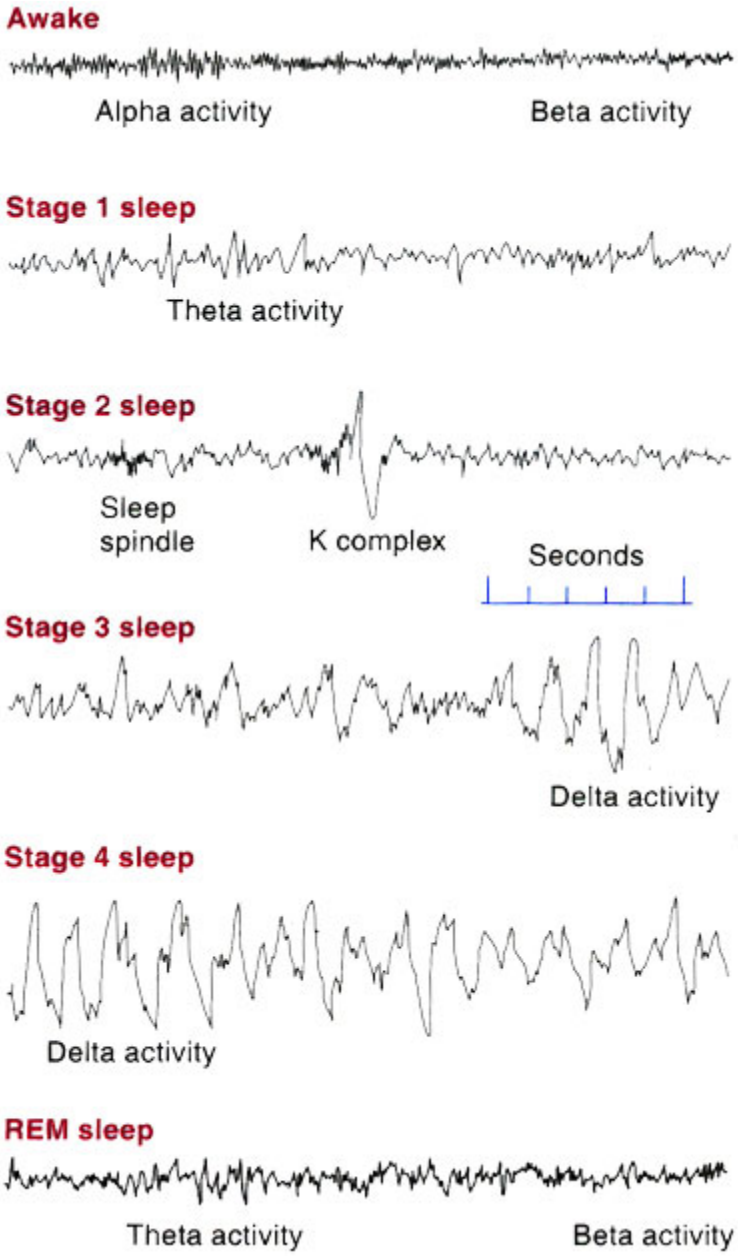


Figure 3: EEG signals for different stages of sleep (Horne 1989)

REM sleep is the stage of sleep where rapid eye movements can be observed, and where dreams occur most frequently. The breathing pattern in REM sleep is usually unstable. The muscle tone tends to decrease significantly during REM sleep, to resemble a state of muscular paralysis.

Normal sleep involves a cycling through stages 1, 2, 3 and 4 of NREM sleep, followed by a REM stage approximately every 90 minutes. As the night progresses, the deeper stages are no longer observed, and more time is spent in REM sleep. A graph of sleep stage versus time is known as a hypnogram, and an example is shown in figure 4 below. The sleep-wake cycle is mainly controlled by a combination of the circadian clock in the suprachiasmic nucleus of the brain, and a sleep drive which depends on the previous time spent awake and the time and quality of sleep (Douglas, 2002).

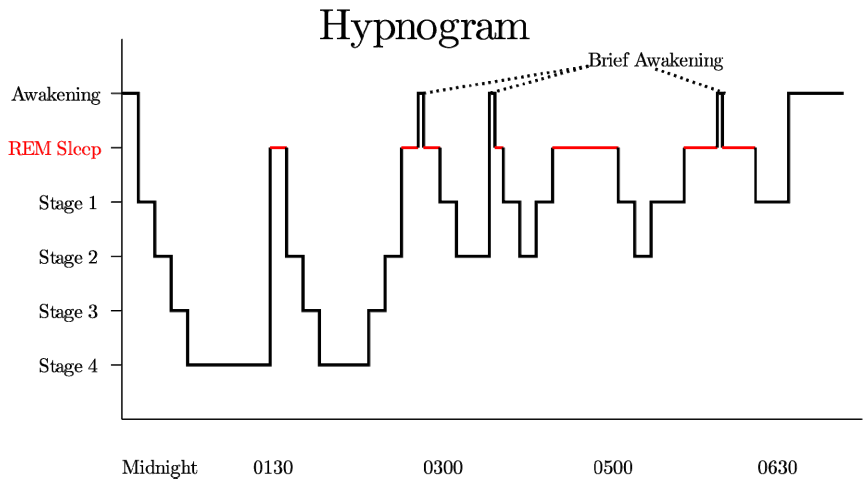


Figure 4: A hypnogram showing sleep stages over a 7 hour period (http://en.wikipedia.org/wiki/Sleep)

2.3 Physiology of the breathing drive during sleep

One of the considerations in this thesis is about how to stop a sleep apnea episode without actually wakening the patient. Thus, it is useful to consider how the respiratory drive operates during sleep, and how a transient awakening causes the breathing to restart. Ideally, in a successful treatment, we would want to be able to re-start the breathing without the need for a transient awakening.

2.3.1 Sleep/wake control by the reticular activating system

The reticular activating system (RAS) in the brain is associated with the control of wakefulness, and appears to function as a gateway to sensory information. It monitors and adjusts incoming and outgoing nerve signals to influence how the associated functions are performed. The location of the RAS in the brain is shown in

figure 5 below, and it includes the reticular formation, located in the pons and mid-brain area of the brainstem, along with its connections to other parts of the brain.

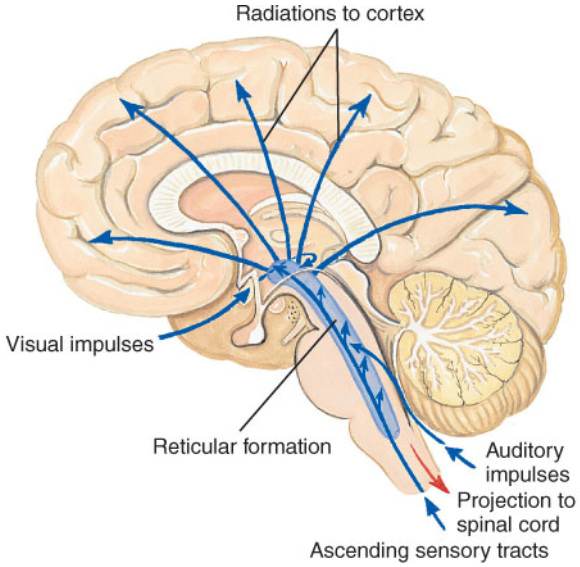


Figure 5: The reticular activating system (Thibodeau and Patton, 2007)

In addition to control of wakefulness, the RAS influences respiration and other critical body functions such as circulation. Stimulation of the RAS suppresses slow cortical waves (0.3–1 Hz), delta waves (1–4 Hz), and spindle wave oscillations (11–14 Hz), which correspond to sleep states, and promotes gamma wave oscillations (20 – 40 Hz), which correspond to a state of wakefulness (Burlet 2002). Inhibition of the RAS occurs during sleep. During a sleep apnea episode, the decreased oxygen and increased carbon dioxide levels in the blood trigger an activation of the RAS, resulting in a transient arousal.

2.3.2 The respiratory centre in the brainstem

The respiratory centre, which controls the automatic respiratory drive, is also located in the brainstem. The respiratory centre controls breathing automatically while a person is in NREM sleep. If no physical airway blockage is present, breathing can be restarted by increased neurogenic activity at the respiratory centre.

A diagram of the brainstem, with various parts of the respiratory centre illustrated, is shown in figure 6 below. The ventral and dorsal respiratory groups in the medulla initiate and maintain breathing rhythms, and they send nerve impulses to signal the

reflex opening of the larynx and movements of the rib cage muscles and diaphragm. This expands the chest cavity, creating a partial vacuum to draw air into the lungs.

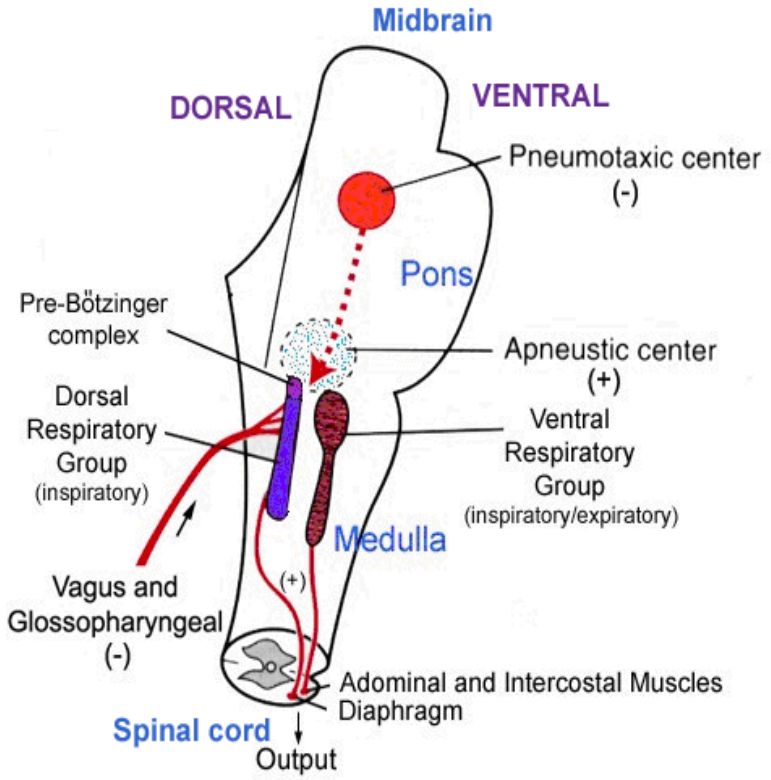


Figure 6: Parts of the respiratory centre in the brainstem. (adapted from http://www.colorado.edu/intphys/Class/IPHY3430-200/015breathing.htm)

The ventral and dorsal respiratory groups in the medulla are controlled by the apneustic centre in the lower pons. The apneustic centre produces inspiratory spasms, which if uninterrupted, would be of a prolonged duration. The apneustic centre is believed to be closely associated with neurons in the reticular activating system (RAS), although the exact processes involved are not clear. In a healthy person, the apneustic centre is restrained by impulses from the vagus nerve and from the pneumotaxic centre, located in the upper third of the pons. The pneumotaxic centre cyclically inhibits inspiration. During inhalation, the inflation reflex activates stretch receptors in the lungs. This causes afferent nerve impulses to travel up the vagus nerve and directly to the apneustic centre, in order to limit the inhalation time (Comroe 1974).

Carbon dioxide levels are the most important factor in stimulating the respiratory centre. When carbon dioxide levels become too high, this state is known as hypercapnia. Central chemoreceptors (not shown in figure 6 above) for detecting carbon dioxide levels in the cerebral spinal fluid (CSF) are located on the lateral surfaces of the upper part of the medulla, but separate from the respiratory centre. These chemoreceptors don't respond directly to changes in carbon dioxide partial pressure, but instead, they respond to the resulting changes in hydrogen ion concentration, i.e. changes in pH, in the CSF. The signal from these chemoreceptors during hypercapnia leads to the respiratory centre increasing the breathing rate. According to Nattie & Li (2009), multiple brain stem sites are responsible for central chemoreception, and other chemical changes are detected in addition to the hydrogen ion changes resulting from increased carbon dioxide levels. One part of the central chemoreceptor region of the medulla is the Pre-Bötzinger Complex (shown in figure 6 above). The Pre-Bötzinger Complex is sensitive to hypoxia (Solomon et al 2000) and is responsive to a number of different neurotransmitter chemicals, providing a mechanism by which opioid drugs can inhibit breathing.

In addition to the central chemoreceptors in the medulla, and the stretch receptors in the lungs, as discussed above, sensors in other parts of the body also have an effect on respiration. Blood oxygen levels are detected by peripheral chemoreceptors in the carotid bodies, located in the carotid arteries of the neck, as shown in figure 7 below. These peripheral chemoreceptors are sensitive to oxyhaemoglobin saturation in the blood, and they enable the carotid bodies to pass nerve impulses to the respiratory centre, indicating changes in blood oxygen levels. If the blood oxygen significantly decreases (a state known as hypoxemia), nerve impulses are sent from the carotid bodies via the vagus and glossopharyngeal nerves to the respiratory centre, in order to stimulate breathing.

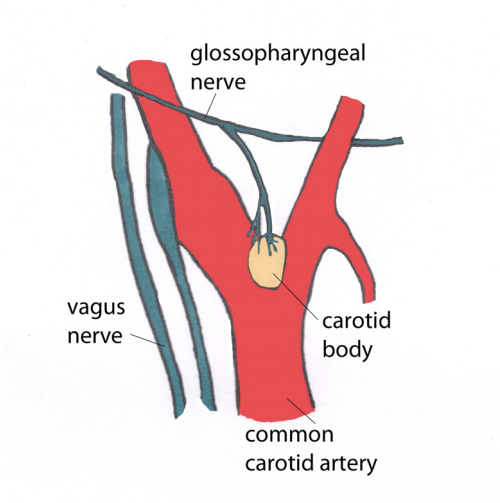


Figure 7: Carotid body in the carotid artery of the neck

The respiratory centre also receives signals from baroreceptors in the aortic arch, airflow and pressure sensors in the upper airway, proprioceptors in the muscles and joints (which are particularly important during exercise), and receptors for touch, temperature and pain. Paralysis of the nasal air sensors using local anaesthetic can induce a temporary central sleep apnea, because under normal circumstances, these airflow and pressure sensors provide control signals to the respiratory centre. Ring-like muscles on the pharynx wall are widened on each inhalation, but other ring-like muscles that prevent the walls collapsing are normally activated using signals from the nasal air sensors, and this ceases to happen if the sensors are paralysed.

The automatic mechanism described above relates to control of breathing during the various stages of NREM sleep. Failure in the automatic system may occur if the communication of the nerve signals to the respiratory centre is disrupted or if the cells receiving these signals are damaged so that they cannot correctly process the incoming sensory information. However, such damage does not affect the patient during wakefulness, because a different mechanism is then responsible for breathing control, involving a different part of the brain. In pure central sleep apnea, the automatic breathing mechanisms are not functioning correctly, so a person may be able to breathe without any problem while awake, but have difficulty in breathing during sleep.

2.3.3 The conscious control of breathing

When a person is awake and also during REM sleep, the "voluntary" respiratory area of the cerebrum has a key role in the control of breathing. Breathing is thus partly under conscious control, although this conscious control is limited. For example, if a person tries to hold their breath for too long, the automatic breathing mechanism takes over and restarts the person's breathing to prevent suffocation. In a condition known as the Ondine Curse, a person can breathe as long as they consciously think about it, but they are unable to breathe automatically, due to damage to the automatic mechanism (Dement 2000).

As the patient's carbon dioxide level increases and oxygen decreases during a sleep apnea episode, the wakefulness mechanism is activated and breathing may resume under control of the voluntary system, to prevent suffocation during sleep. In a related sleep disorder known as "upper airway resistance syndrome", slight reductions in airflow cause the wakefulness mechanism to be activated, but without an actual cessation of breathing.

The "voluntary" respiratory area has a lower sensitivity to carbon dioxide levels and oxygen levels than the brainstem's automatic mechanism, and takes longer for activation. Some people have sleep apnea episodes only during NREM sleep, and others have sleep apnea episodes only during REM sleep, which may be a result of the particular part of the nervous system that is malfunctioning. Often, when sleep apnea occurs in both NREM and REM sleep, it is worse during the REM sleep.

In a condition called Cheyne Stokes respiration, the neurological feedback mechanisms to monitor carbon dioxide levels do not react quickly enough, and the result is cyclical breathing. Even while the patient is awake, the breathing varies between very fast breathing and a cessation of breathing, instead of maintaining a regular respiratory rate. This is similar to high altitude periodic breathing. When the breathing is stopped, there is no respiratory effort made by the patient. The faster breathing later in the cycle allows excess carbon dioxide to be expelled and extra oxygen is absorbed to compensate for the breathing cessation. Cheyne-Stokes

breathing is commonly seen in patients with congestive heart failure (AASM 1999), and such patients commonly also have central sleep apnea.

2.3.4 The effects of hypoxemia and hypercapnia

In a sleep apnea patient, severe hypoxemia can occur, with blood oxygen levels dropping by as much as 50%. The lack of oxygen results in cyanosis, where the patient's skin turns blue, especially at the extremities. A build up of carbon dioxide (hypercapnia) also occurs, resulting in respiratory acidosis. The acidosis is followed by the release of vasoactive agents into the bloodstream, for example, prostacyclin, thromboxane, endothelin and arginine-vasopressin. When these reach the myocardium, they have the effect of increasing the myocardial oxygen requirements. This leads to increased afterload of the left ventricle, and may eventually result in left ventricular hypertrophy.

Eventually, as the sleep apnea incident progresses, a transient arousal from sleep is triggered. On restoration of the airway, the patient typically takes several gasping breaths to restore their blood oxygen levels. The heart then works excessively hard to pump the newly oxygenated blood round the body. Transient systolic blood pressures as high as 300 mmHg have been measured at this time, which is extremely high compared to the normal 110-120 mmHg levels (Dement 2000). These extremely high blood pressures occur many times per hour, night after night. High blood pressure is known to cause many damaging effects, including cardiac damage and arrhythmias, cardiovascular disease, damage to the other organs, seizures, and small strokes in the brain. Heart failure can occur if the cardiac arteries are already partly blocked.

The link between episodic night time hypertension and permanent pulmonary hypertension is not well understood. Brooks et al (1997) found that acute and transient increases in the night-time blood pressure eventually produced sustained daytime hypertension. However, Weitzenblum & Chaouat (2005) found that during obstructive sleep apnea, only the transmural pulmonary arterial pressure (PAP) provided reliable measurements, increasing throughout the apnea episodes due to hypoxic vasoconstriction, and decreasing after breathing has resumed. They found

that daytime hypoxemia, generally due to an associated chronic airflow obstruction, is the major cause of permanent pulmonary hypertension, and that nocturnal hypoxemia is less significant. The intravascular pulmonary arterial pressure was observed to return to control levels if several minutes of normal ventilation occurred, but it gradually increased during a period of repeated sleep apnea episodes. A differing view is provided by Duran-Cantolla et al (2009), who showed that intermittent hypoxemia (such as in sleep apnea), renin–angiotensin system, chemoreceptor stimulation and sympathetic activation can all lead to systemic hypertension. They discussed animal studies suggesting that sympathetic activity is probably the most important factor leading to high blood pressure (Duran-Cantolla, 2009).

Figure 8 below, from Duran-Cantolla (2009), shows a summary of the mechanisms and factors behind arterial hypertension, including the effects of various risk factors.

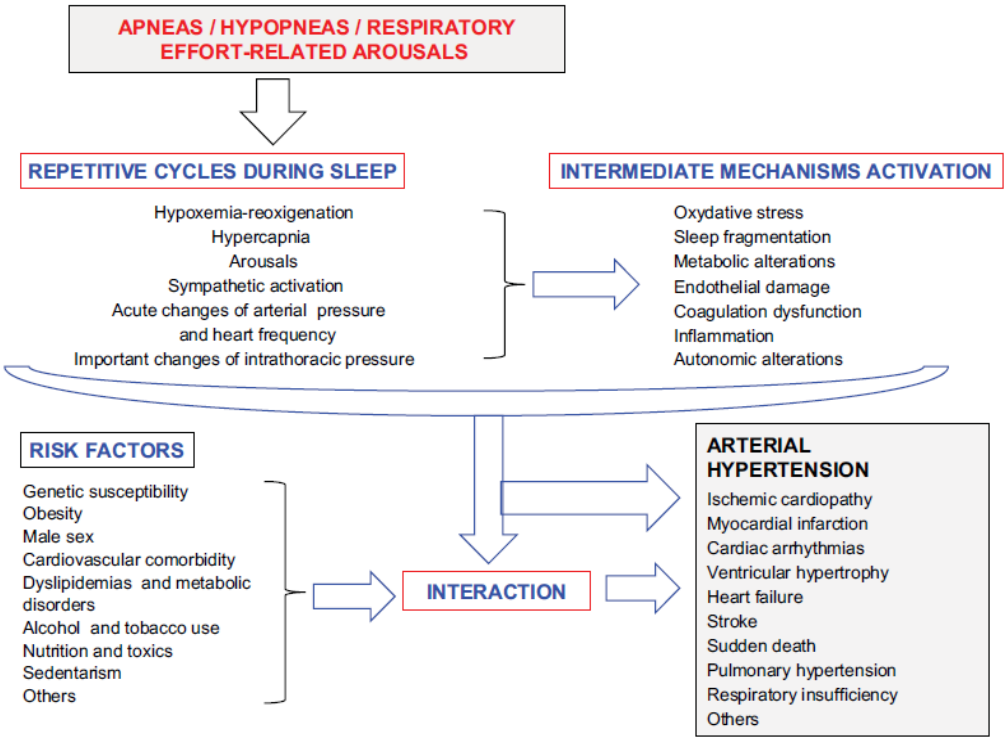


Figure 8: Hypertension mechanisms (Duran-Cantolla 2009)

2.3.5 Arousals in sleep apnea

Falling oxygen levels in blood causes activation of the reticular activating system (RAS), and this is known to arouse the person from sleep, restoring muscle tone and activating the sympathetic nervous system. Ayappa & Rapoport (2003) suggest that although sufficient levels of hypoxia and hypercapnia will arouse most people, it is the mechanical effort that is largely responsible for arousal in OSA. They discussed data from Gleeson et al (1990) showing that arousal always occurs at the same level of interthoracic pressure swing in a given patient. However, in central sleep apnea, there is no respiratory effort, and the hypoxemia and hypercapnia must therefore be responsible for the arousal.

Mendez et al (2008) performed time-frequency analysis of the heart rate variability (HRV) during arousal from sleep, with and without EMG activation, using five healthy obese subjects. They used three different time-frequency representations to obtain energy distribution and spectral indexes during the arousal episodes. Arousals with chin activity showed stronger changes in the RR intervals and in the LF component (which is related to sympathetic activity) and this was statistically different than for arousal without the chin activity. They concluded that there is a more evident stress for the heart when an arousal is related to external muscular activity.

It is the lack of breathing that ultimately causes the arousal, regardless of whether the mechanism is due to mechanical effort or hypoxemia and hypercapnia. If a sleep apnea intervention treatment is able to prevent significant hypoxemia and hypercapnia, but wakens the patient in the process, then it may still provide some health benefits. However, the viability of such a treatment may depend on just how frequently it causes the patient to awaken, and whether the awakenings were to a fully conscious state, or were just short micro-arousals. It is highly desirable to avoid repeated awakenings, because this could lead to excessive activation of the sympathetic nervous system, causing, disturbances in hormone levels. Hormonal disturbances can lead to metabolic disorders developing in the long term, e.g. diabetes mellitus and obesity. A further disadvantage of arousals is that they may

actually increase the airflow to unnecessarily high levels at the time when the upper airway opens (Trinder 1997).

Another issue is whether it is physiologically necessary for an arousal to take place, in order to restore the airway and the breathing, and whether it is possible to avoid the sympathetic activation that normally accompanies an arousal. The National Sleep Foundation defines a micro-arousal as a change in sleep state to a light stage of sleep. According to psychosomaticmedicine.org a micro-arousal is “a sudden transient cortical activation during sleep", but does not necessarily result in a behavioural awakening. Thus, micro-arousals may not necessarily involve full changes in the EEG state to wakefulness, but may involve a temporarily change to a state of light sleep. Although arousals may be generated in response to sensory perturbations, such as respiratory interruption (apnea or snoring), alteration of heart rate or blood pressure, noise, or movement disorders, it is not uncommon for healthy people to have micro-arousals. However, sleep apnea patients have many more micro-arousals than healthy people.

According to Younes (2004), in 17% of apnea episodes, arousal may not actually occur. More investigation into the mechanisms involved is desirable, including the thresholds required for sympathetic activation.

3. Diagnosis of Sleep Apnea

Various techniques have been used to detect sleep apnea, both in a clinical setting and experimentally. This section provides a review of such techniques.

3.1 Polysomnography

Polysomnography is the most common clinical method of diagnosing sleep apnea. It involves the patient sleeping overnight in a sleep laboratory, where multiple physiological parameters are measured and the apnea/hypopnea index (AHI) can be calculated from the results, giving a quantitative indication of the severity of the sleep apnea. Polysomnography is considered the "gold standard" for diagnosis of sleep apnea. The measurements taken during polysomnography generally include the following (van Houwelingen, 1999):

- Electrocardiogram (ECG), which also gives pulse transit time and heart rate variability (HRV) data
- Electroencephalogram (EEG) is used to confirm the time and occurrence of different sleep stages, arousal levels and states of consciousness, rather than to detect sleep apnea episodes directly.
- Electroculogram (EOG), using electrodes placed at the corners of the eyes, to detect rapid eye movements in REM sleep and slow eye movements during NREM sleep
- Electromyogram (EMG), often using electrodes placed on the chin, for detecting changes in muscle tone and activity, to indicate the stage of sleep
- Blood oxygen saturation, via pulse oximetry measurements which are usually taken on the fingertip or earlobe
- Airflow, e.g. using nasal pressure measurements or pneumotachography or using thermistors under the nose or mouth to monitor changes in air temperature which indicate any change in breathing patterns
- Respiratory effort, e.g. using RIP (respiratory inductive plethysmography), or using a belt with a strain gauge attached around the chest or abdomen.
- Body position, e.g. by recording with a video camera
- Body movements, e.g. leg movement can be detected using EMG

- Sleep sonography, to record sounds made by the patient during sleep.

The data is collected under the supervision of a skilled technician, who monitors the patient for the duration of the study. The polysomnography results are interpreted manually by experts, rather than by an automated process on a computer. Thus, polysomnography is a very thorough process, which aims to maximise the quality of the results.

However, there are some disadvantages to polysomnography. It is expensive, due to the need for an overnight stay in a sleep laboratory, the highly trained staff that are needed, and the cost of the specialist monitoring equipment. It is lengthy, as it takes at least a full night to obtain the measurements. Polysomnography can be uncomfortable and inconvenient for the patient, as it is difficult to sleep normally in a clinical environment whilst being monitored with various probes and wires. The results obtained may not be fully representative of the patient's normal sleep. This can lead to inaccuracies in the diagnosis, or the need for further nights of study, which increases the cost and inconvenience. It is highly desirable to have a lower cost and more convenient method of diagnosis, which is also extremely reliable and accurate.

In recent years, portable monitors are becoming increasingly available for recording a subset of the data that is measured in a full polysomnography session (de Oliveira et al, 2009). For example, a portable monitor may measure heart rate, blood oxygen saturation, nasal airflow, respiratory effort and body movements. Portable monitors can be extremely useful, as they can be taken into a home environment, and they are less expensive to operate and maintain, because they measure a smaller number of parameters. However, they may give false and misleading readings if a sensor becomes detached during the night, and they are less useful for high risk patients who require to have trained medics on hand.

The AASM study of 1999 (AASM 1999) classified different diagnostic measurement techniques, according to their effectiveness and reliability, where recommendation

grade 'A' means good to excellent, 'B' means limited information available, 'C' means very little or no research available, and 'D' means not recommended. The gradings are shown in figure 9 below.

Event/Condition	Method of Measurement	Recommendation Grade*	Quality of Evidence†
Obstructive Hypopnea/ Apnea	1. Pneumotachometer	A	1
	2. Nasal Pressure	B	2a; 2b
A hyponea/apnea is assumed	3. RIP — sum channel 50% decrease from baseline	B	2a; 2b
to be obstructive unless criteria	4. RIP — dual channel 50% decrease from baseline	C	3
for a central event are met	5. RIP — single channel	C	3
	6. Piezo sensors, Strain gauges, Thoracic impedance	C	3
	7. Thermal sensors	D	3
	8. Expired CO_2	D	3
	9. Measurement of breathing <50% (but clear) decrease from baseline with 3% O_2 desaturation or arousal	B	2a
Respiratory Effort Related Arousal	1. Esophageal pressure	A	1
	2. Nasal pressure	C	3
	3. Supraglottic pressure	C	3
	4. Diaphragm EMG	D	3
Central Hypopnea/ Apnea	1. Esophageal pressure/Pneumotachometer	A	1
	2. RIP	C	3
To distinguish from an	3. Diaphragm EMG	C	3
obstructive apnea	4. Oronasal airflow (Thermal, Expired CO_2) sensors	D	3
	5. Piezo sensors and Strain gauges	D	2a
Cheyne-Stokes Breathing	1. Esophageal pressure/ Pneumotachometer	A	1
	2. RIP	B	3
	3. Diaphragm EMG	C	3
	4. Oronasal airflow (Thermal, Expired CO2) sensors	D	3
	5. Oximetry	D	3
Sleep Hypoventilation	1. $PaCO_2$	A	1
	2. O_2 desaturation (unexplained)	B	3
	3. $TcCO_2$	C	1
	4. Calibrated RIP	D	2a
	5. Expired end tidal CO_2	D	1

Figure 9: Table showing comparison of measurement methods (AASM 1999)

The following sections describe some of the measurements taken in polysomnography in further detail.

3.2 ECG and heart rate variability (HRV)

ECG measures the electrical activity of the heart. A typical ECG waveform is shown in figure 10. The time between heartbeats is known as the R-R interval, as shown.

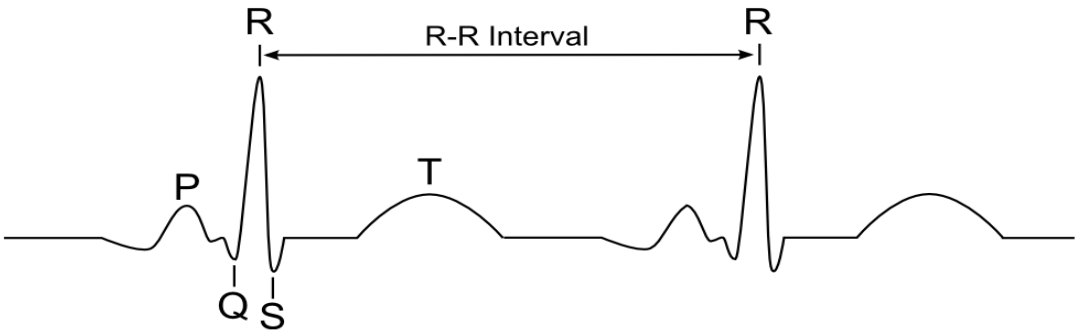


Figure 10: Typical ECG waveform showing R-R interval

The beat-to-beat variation is known as the heart rate variability, and this can be determined by the intervals between successive R-wave peaks in the ECG signal. It is well-established that HRV provides a good indicator of the occurrence of sleep apnea. This is because heart rate is largely controlled by the autonomic nervous system. Sympathetic activity speeds up the heartbeat (thus decreasing the R-R intervals) and parasympathetic activity decreases the heartbeat (thus increasing the R-R intervals). Normally, during sleep, the parasympathetic branch is dominant. However, when a person has a sleep apnea episode, followed by an arousal, the sympathetic branch is activated, and the heart rate increases as a result. Monitoring the HRV can thus provide an indication of changes in nervous system behaviour, which can indicate a sleep apnea episode. The heart rate rises during apnea and rises further at apnea termination. It then varies significantly during arousal.

For the above reasons, there has been a great deal of interest in further research to predict sleep apnea episodes from ECG signals alone. Also, HRV is a relatively straightforward parameter to compute, as automatic signal processing could be used to identify the QRS complex and determine the R-R intervals. In particular, analysis of the spectral components of HRV was found to give a good indicator of sleep apnea episodes, because these correlate well with sympathetic or parasympathetic activity. The three major spectral components are:

(i) a high frequency oscillation centred on the breathing frequency, known as a "respiratory sinus arrhythmia" (RSA), and related to parasympathetic activity;

(ii) a low frequency oscillation related to baroflex dynamics, related to sympathetic activity; and

(iii) a very low frequency oscillation that may be related to thermoregulation and low frequency periodicities in respiration.

In 2000, the "Physionet/Computers in Cardiology Challenge 2000" competition was run by Physionet and Computers in Cardiology to write an algorithm to detect sleep apnea in a number of sleep recordings, and the accuracy was scored according to a minute by minute epoch based approach (Penzel et al 2002a). Many different signal processing techniques were used, including Short Term Fourier Transforms, wavelets, and autoregressive spectrogram. Some of the algorithms were over 90% successful in diagnosis.

The use of HRV instead of a full 12-lead ECG would make monitoring more straightforward in a home environment. A simple chest belt, e.g. similar to those used in heart rate monitors for fitness training, would be easy and inexpensive to provide. Measuring HRV in this manner increases the noise, artefacts and effects of patient movement on the signal, making successful detection more challenging. However, Mendez et al (2009) demonstrated the possibility of sleep apnea screening by autoregressive models from a single ECG lead.

Despite the successes of HRV detection and analysis in sleep apnea diagnosis, the methods used were based on retrospective analysis of pre-recorded data, and real-time processing was not a consideration. It is now believed that HRV is not a good variable for sleep apnea detection in real-time because it does not change quickly enough after the start of a sleep apnea episode (Robertson, 2009). For example, it can take over a minute for a detectable change in HRV after the patient stops breathing. By the time the HRV signal is indicating a problem, the damage is already done. The patient has already experienced hypoxemia, hypercapnia, sympathetic nervous system activation and a transient arousal from sleep. Thus, for a treatment involving intervention based on real-time detection of sleep apnea, HRV is not a good candidate.

It is not apparent whether there may be other information that could be extracted from an ECG waveform to indicate a sleep apnea episode at an earlier stage. If the only mechanism by which the ECG signal changed in response to sleep apnea was the sympathetic nervous system activation, it would be likely that any detectable change would come too late. However, another approach may be ECG-derived respiration, where the ECG signal is used to calculate chest movements. Moody et al (1985) and Bianchi et al (2003) provide discussion on the use of HRV to estimate respiratory signals. Although ECG provides a less accurate measurement of respiratory signals than direct methods, it has the advantage that it doesn't actually interfere with respiration, and it may be a lot more comfortable for the patient.

ECG Derived Respiration (EDR) involves calculating movements of the heart and changes in its position over time, using the ECG signal received at different ECG electrodes. This indicates how the lung volume changes over time. During a sleep apnea episode, a reduction in the EDR waveform would be observed. Some authors (Mazzanti et al, 2003) have found EDR to be insufficient for sleep apnea detection, due to noise and lack of sensitivity. Other authors (Pu et al, 2003) have found large fluctuations in EDR, and have proposed that a better quantitative index of EDR is needed in order to pick up the irregularities.

3.3 Pulse oximetry

Pulse oximetry involves measuring arterial oxyhaemoglobin saturation (SaO_2) by transmitting light through the skin, usually in the fingertips or earlobes, and measuring how much of the light is absorbed (Martinez, 2005). A red light emitting diode (LED) of wavelength 660nm and an infra-red LED of wavelength 940nm are positioned on one side of the patient's fingertip or earlobe, and a light detector is placed at the opposite side. Reduced haemoglobin absorbs more red light than oxyhaemoglobin, and oxyhaemoglobin absorbs more infra-red light. The ratio of absorbed red and infra-red light allows the proportion of oxyhaemoglobin to be determined. Figure 11 below shows an example of a finger pulse oximeter device.

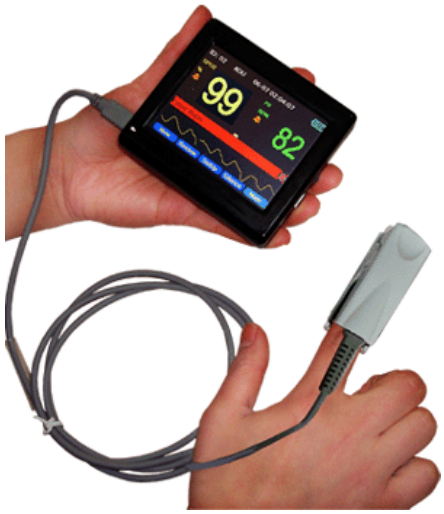


Figure 11: A finger pulse oximeter, by CONTEC Medical Systems Co., Ltd

For a healthy adult, the SaO_2 is usually over 97%. However, the oxygen saturation may drop much lower than this in patients with sleep apnea. In severe sleep apnea, the oxygen saturation can drop below 50% (Lipman, 1990). Figure 12 below shows the blood oxygen saturation of a sleep apnea patient over a 2 hour period, using data from the Physionet physiologic signal database (www.physionet.org). The data was from the apnea-ecg data set (Physionet file: a01r, 0-120min), and it was imported into Matlab, and plotted.

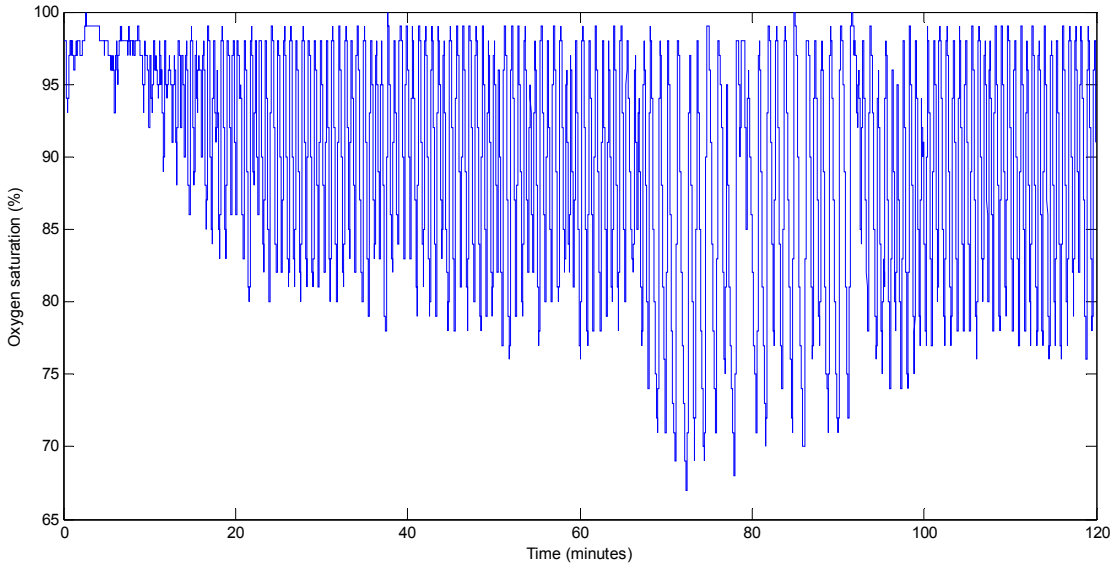


Figure 12: Oxygen saturation data for a sleep apnea patient

For this patient, the short-term average oxygen saturation tends to decrease over the first 70 minutes, dropping as low as 65%. Even higher drops are seen over the following approximately 20 minutes. This pattern may be a result of the 70-90 minute period corresponding to the REM sleep stage. The sleep cycle would then return to NREM sleep at the end of this period, with a corresponding adjustment in oxygen saturation levels.

Pulse oximetry is well established as suitable for home monitoring and diagnosis of sleep apnea. It is cost effective and accurate. It can also allow monitoring of the pulse rate. However, it is not suitable for real-time measurements, because the blood oxygen levels can take up to several minutes to change after the start of the breathing cessation. A time lag of at least 10-60 seconds is normal. Also, it does not detect excess carbon dioxide (hypercapnia), which can as a result be overlooked in some patients. Pulse oximetry provides no information on the total amount of haemoglobin present, but only on the proportion of haemoglobin which is in the form of oxyhaemoglobin.

A pulse transit time (PTT) can be determined using both a pulse oximeter and an ECG signal, and this indicates the time it takes for a pulse wave to move from the aortic valve (as detected by ECG) to the periphery (as detected by pulse oximetry). The PTT is inversely proportional to arterial blood pressure, which falls during inspiration and rises during expiration. The PTT thus allows the breathing pattern to be determined, and it may be an affective alternative to airflow measurements for sleep apnea detection (Pitson et al 1995, Smith et al 1999). However, as in HRV and pulse oximetry, there is a delay between a sleep apnea event and any detectable change in response. This technique is also susceptible to artefacts from movement.

Peripheral Arterial Tonometry (PAT) uses a finger pneumo-optic plethysmograph to measure blood flow changes in the arteries of the finger. In OSA patients, the pulse waveform decreases transiently with a timing and periodicity that is linked to the oxygen levels in the arterial blood. However, instead of simply measuring the blood oxygen levels, as in pulse oximetry, PAT measures the amount of blood flowing

through the arteries of the finger. Blood flow in these peripheral arteries gives a sensitive indication of the level of activation of the autonomous nervous system. O'Donnell et al (2002) and Penzel et al (2002b) discuss correlation and reliability of PAT, and it was found to provide 80% accuracy in sleep apnea detection. PAT has a timing delay, and is thus unsuitable for real-time measurements.

3.4 Air flow measurements

It is possible to measure airflow in a number of ways. A pneumotachometer is a device which measures a very small pressure drop within a short tube of exhaled air, in order to quantitatively measure the tidal volume and direct airflow during breathing. It uses a sealed face mask with a pneumotachometer. However, it is intrusive and uncomfortable for the patient, thus not suitable for monitoring on a frequent nightly basis in a home environment.

Nasal prongs may be used with thermistors or thermocouples to detect temperature changes in inhaled versus exhaled air, thus detecting the breathing cycle. This has several difficulties - it is non-linear, with limited sensitivity, and the equipment is easily displaced from the patient's nose during sleep. The prongs can cause nasal obstruction that actually encourages mouth breathing. Non-invasive nasal cannulas or pressure transducers are harder to calibrate and can give false positives due to mouth breathing.

Optovent technology involves an optic fibre sensor for real-time monitoring of air flow, by measuring humidity of exhaled air. Real-Time Respiration RtR^{TM} technology measures differences in temperature and humidity between inhaled and exhaled air, using an IR sensor. This allows the exhaled carbon dioxide levels to be calculated, in a manner that is not susceptible to motion artefacts.

The Sleepstrip^{TM} (shown in figure 13 below) is a small, lightweight device, worn above the upper lip and below the nose, for monitoring airflow. It has oral and nasal thermistors, and real-time analysis hardware and software to allow detection of air temperature changes and calculate the airflow accordingly. After a 20 minute

calibration period, any decrease or cessation of breathing is detected and counted during the night, for a period of at least five hours. The number of respiratory events per hour is displayed on a miniature chemical display unit.

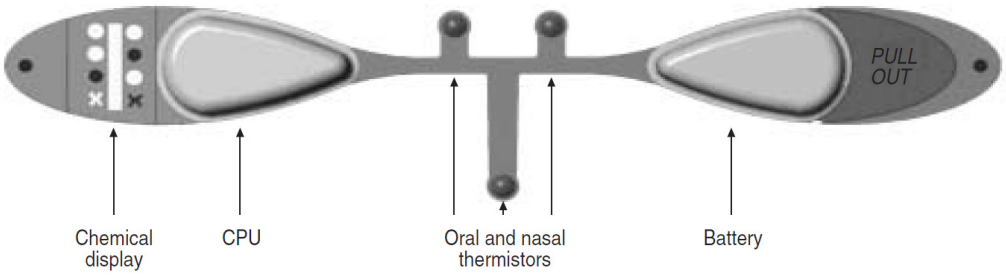


Figure 13: The Sleepstrip™ (Shochat et al, 2002)

The Sleepstrip™ is not intended to replace a full polysomnography study of a patient, but it provides a low cost and easy to use screening method to allow patients with the most severe sleep apnea to be identified and prioritised first for urgent treatment (Shochat et al 2002).

In her 2009 EngD thesis, Helen Robertson discussed the use of neural networks to classify nasal airflow measurements, for real-time identification of sleep apnea episodes (Robertson, 2009). She found that nasal airflow monitoring was more successful for real-time sleep apnea detection, because it is possible to detect the very beginning of a sleep apnea episode. Robertson's work showed that it was even possible to predict the start of a sleep apnea episode before it actually started, by identifying irregularities in the sinusoidal breathing signal in a number of inspirations before the sleep apnea onset. The prediction could be made from even a single breath, using a 5 second, 2.6 second or 2 second recorded sequence with 10Hz sampling rate. The signals were normalised, analysed using principal component(s) analysis (PCA) and classified with a neural network. Empirical mode decomposition (EMD) as described by Huang et al (1998) is an alternative technique that could also be used. Traditional spectral analysis was not sufficiently effective, because it requires a signal that is stationary or periodic and linear, and these conditions were not fulfilled.

3.5 Respiratory effort

Plethysmography is a method of detecting volume changes in the chest, thus indicating a patient's breathing pattern. Impedance pneumography uses a 50-500kHz AC current to record thoracic movements or volume changes. Respiratory Inductive Plethysmography (RIP) has a higher accuracy than impedance pneumography, and uses a 300kHz current to detect changes in the cross sectional area of the rib cage and abdominal compartments. RIP is one of the best non-invasive tools currently available. RIP may be implanted on a chest belt or abdomen belt. A wearable garment called Lifeshirt® has been developed to measure R-R intervals and to perform RIP measurements, from which various respiratory parameters are derived (Derchak 2007).

There are several problems with plethysmography. It doesn't actually measure volume, but only a change in volume. Thus, it is difficult to calibrate and achieve stable signal polarity. It is susceptible to motion and cardiogenic artefacts. Signal degradation occurs due to changes in body position. It is also hard to clearly distinguish between obstructive, mixed and central sleep apnea.

Thoraco-abdominal movements may also be monitored to indicate the respiratory effort. This can indicate the difference between OSA and CSA. A belt with a strain gauge or pressure transducer may be used. A lack of synchrony between the thorax and the abdomen can indicate upper airway obstruction. However, it is difficult to standardise this method due to variations in body position, sleep stage and obesity, and it needs accurate calibration (Smith et al 1999), which is difficult to achieve.

Another "wearable garment" approach is the Somnus nightshirt for monitoring sleep, as shown in figure 14 and discussed at the following website:
http://www.technologyreview.com/biomedicine/37606/?mod=related.
The nightshirt garment is a snug fit on the patient, and contains capacitive elements which stretch with the patient's breathing movements. The signals are analysed with a built-in controller to classify the patient's sleep into different sleep stages.

Figure 14: The Somnus nightshirt for sleep monitoring

3.6 Electromyogram (EMG)

EMG has been used to detect diaphragmatic movement, but this alone was not found to be sufficiently accurate, and is not recommended by the AASM. Other options include measurements from other respiratory muscles, and genioglossius EMG.

3.7 Audio measurements

Spectral component analysis of snoring sounds can indicate the onset of a sleep apnea episode (Fiz et al, 1996). Very loud snoring is often a warning sign, although it is debatable whether or not snoring on its own is sleep disordered breathing. Snoring is caused by vibrations of the soft tissues of the pharynx, soft palate and uvula, and can be associated with pressure swings in the oesophagus.

Phonocardiography is where heart signals are measured with an electret microphone attached to a precordial stethoscope. In a study by Reed et al (2001), wavelet decomposition was used, along with classification using a neural network, to enable recognition of 5 different heart diseases from the detected sound signals. However, there do not appear to be any studies specific to sleep apnea. The use of electret microphones in air coupling capsules has also been discussed by Kahya (2003a, 2003b), Gross et al (2003) and Sen (2003).

3.8 Summary

There is a need for a more accessible and comfortable method of real-time detection and monitoring of sleep apnea. Many of the above-described techniques have an

associated time delay which precludes real-time detection. In a device for detecting and interrupting sleep apnea episodes, a minimal time lag in the detection of breathing cessation is vital. A technique discussed above that is particularly suitable for real-time detection is nasal airflow. However, this would be impractical in a device to be worn nightly, because it is too invasive and not sufficiently comfortable to the patient. Also, it is susceptible to error due to mouth breathing, and it may be displaced out of position relatively easily during sleep. Patients who are unable to tolerate continuous positive airway pressure (CPAP) treatment are unlikely to be able to adapt to the nightly use of a nasal airflow sensor.

The next chapter discusses the use of pressure sensitive mats for monitoring breathing movements, as this may have potential for use in an alternative real-time method of sleep apnea monitoring.

4. Pressure Sensitive Sleep Monitoring Devices

In chapter 3, various sleep apnea detection methods were discussed. None of these methods was completely satisfactory for both reliable real-time measurements and high patient comfort levels. An alternative technique that is much less intrusive than some of the methods previously discussed is the use of a pressure sensitive sensor that sits underneath the patient's mattress, to detect the patient's movements e.g. from breathing, heartbeat or activity. Such a pressure sensitive mat does not need to be attached to the patient's body, and has no direct contact with the patient. It could easily be set up for home use, and would ideally be inexpensive to manufacture. In this chapter, previous developments on pressure sensitive mats are reviewed. Such mats are well-established for use in baby movement monitoring, and have also been used in other aspects of sleep monitoring. In this thesis, we are interested in their potential for use in sleep apnea monitoring of adults.

4.1 Pressure sensors for activity and respiration monitoring

Various different technologies have been used to provide pressure sensors for detecting breathing, heartbeat and body movements of a patient. Some of these are merely concerned with the activity level of the patient, e.g. to determine whether a patient is awake or asleep. Monitoring of the activity level during sleep is known as actigraphy. Sadeh et al (1995) provides a review on actigraphy and its ability to provide useful classification and diagnosis of sleep states and conditions, with early studies going back as far as 1922. Elbaz (2002) discusses wrist actigraphy. One problem with movement actigraphy is that it may tend to give an overestimate of sleep time when a subject is awake with no motion.

Pressure sensitive devices have also focussed on detection and analysis of the patient's breathing and/or heartbeat in a diagnostic setting. Svanborg et al (1990) investigated the effectiveness of sleep apnea detection using combined data from oximetry and respiration movements, compared with results from conventional polysomnography. They used a static charge sensitive bed to measure respiration movements. Periods of obstructive sleep apnea were observed to give a diamond-shaped periodic respiration movement pattern, which was usually accompanied by

greater than 4% oxygen desaturation. Patients who had periodic respiration movements for less than 18% of their total sleep time and an oxygen desaturation index of less than 2 were never found to have an apnea index above 5, but patients with periodic respiration movements for over 45% of their total sleep time and an oxygen desaturation above 6 were found to always have an apnea index above 5. This showed that the respiratory movements and oximetry could provide a useful method of sleep apnea diagnosis. However, Svanborg et al were not concerned with real-time sleep monitoring, but merely with the general ability to diagnose whether or not a patient was experiencing sleep apnea episodes. Their reliance on oximetry measurements as well as the respiration movements would preclude real-time measurement and detection of sleep apnea.

4.2 Bed mattress with Emfit sensor foils

Kortelainen et al (2010) discuss the use of a bed mattress with Emfit sensor foils, to detect a patient's sleep stage (wake, NREM or REM) using measurements of the patient's heart beat interval (HBI) and movement activities. Emfit is a porous polypropylene foil, which includes large internal voids with a permanent electric charge. An applied pressure on the Emfit foil causes a change in thickness of the foil, which alters the internal electric field and causes the foil surface to become electrically charged. This charge can be measured, to determine the applied pressure. Kortelainen et al used a sensor area of 1m x 2m, with 160 electrodes, positioned between two thin foam mattresses, to provide a sensor mattress of about 4cm thickness. The sensor mattress was placed under a normal mattress for recording of pressure measurements. They found that the accuracy could be improved using a multichannel bed sensor and spectral averaging. Although the 160 electrode configuration gave a high special resolution for detection of body movement and position, in fact an 8-electrode configuration provided a good balance between cost, reliability and effectiveness in practice. To analyse the collected data, a time-variant autoregressive model (TVAM) was adopted as a feature extractor, using the HBI data to generate parameters based on the joint probability of HBI features. A hidden Markov model (HMM) was then used as a probabilistic classifier, to determine which sleep stage the patient was currently experiencing. Movement features were

used to allow the detection of wake periods. Using only 2 HBI features and one movement parameter, they obtained an accuracy of 79% ± 9% in wake-NREM-REM classification.

4.3 The Angelcare baby monitoring mat with piezoelectric sensor

For a number of years now, various devices have been available on the market to monitor a baby's movements via a pressure sensitive mat placed under the baby's mattress. However, prior to the late 1980s, such devices had been prohibitively expensive. Millns (1986) developed a cost-effective device which uses a PVC-encapsulated mat with a piezoelectric sensor to detect pressure changes resulting from breathing movements. Millns' device had the advantage that it was less expensive to manufacture and it was less complex than a flexible capacitive transducer used for similar purposes. It relied on compression of a piezoelectric element, similar to those found in simple buzzers or audio alarms, to generate a voltage that indicated any change in applied pressure. In contrast, previous piezoelectric movement detectors used a complex and expensive mechanical assembly to bend a piezoceramic transducer when pressure was applied. Due to its low cost simplicity, Millns' design led to the mass manufacture of pressure sensitive baby movement sensor mats. Millns filed a UK patent for his design in July 1986 (Millns 1986). Millns' patent was purchased by a Canadian, Maurice Pinsonneault, who set up a company called Angelcare to manufacture and market the pressure sensitive mats for monitoring of sick babies.

The structure of the piezoelectric mat is shown in figure 15 below. A standard piezoelectric element is attached to a semi-rigid base portion, so that it rests against a spacer pad attached to a backing piece. The entire assembly is encapsulated by a PVC outer layer.

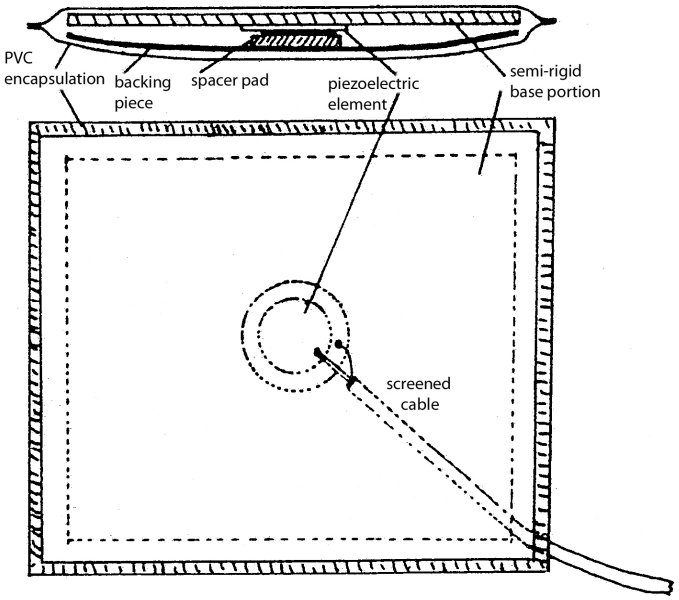


Figure 15: The original Angelcare piezoelectric sensor mat design

The mat works by directing any pressure changes on the top external surface towards the piezoelectric element, which compresses against the backing piece to generate a voltage. The voltage is detected by a controller unit, which is shown as enclosed by the dashed line in figure 16 below.

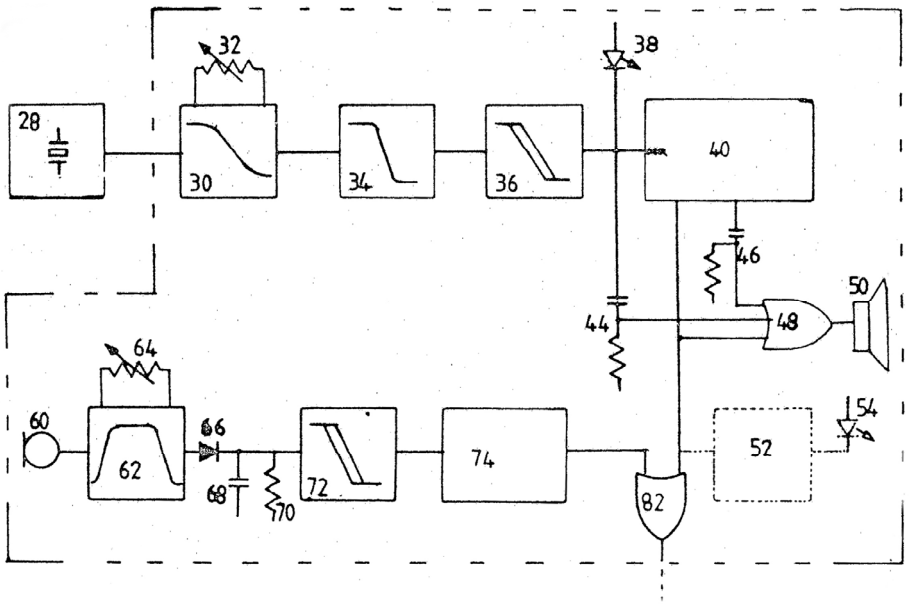


Figure 16: A controller for signal processing in the Angelcare sensor system

The controller unit includes an input, which connects to an output cable from the piezoelectric mat (labelled as 28 in figure 16), to receive a pressure dependent voltage signal. The voltage signal is amplified at a FET pre-amplifier (30), which has a sensitivity adjustment control (32). From there, the signal is filtered by a low pass filter (34) and applied to a Schmitt trigger circuit (36) that is connected to a timer (40). Each time a breathing movement is detected, the timer is reset by means of the Schmitt trigger circuit. However, if the breathing movements are not detected, the timer is not reset, and after a pre-determined time, it triggers an alarm (50) to alert parents or hospital staff. The system also includes an audio circuit to trigger an alarm if the baby's crying is detected by microphone (60) and associated signal processing circuitry.

Maurice Pinsonneault of Angelcare made some further improvements to the design, filing further patents in 1998 and 2001. The 1998 patent (Pinsonneault et al, 1998) related to using an arrangement in which the piezoelectric sensor was attached to a backing plate, and the backing plate was suspended across a cavity in a rigid upper force collector plate. An electrode was provided on the opposite side of the piezoelectric sensor, and the sensor was positioned to press against a semi-rigid spacer element attached to a second rigid plate. When force is applied, the piezoelectric transducer is able to flex, because its central part can bend into the cavity. The semi-rigid spacer element concentrates forces onto the piezoelectric transducer. The result is a detector with higher sensitivity. The structure of this detector is shown in figure 17 below.

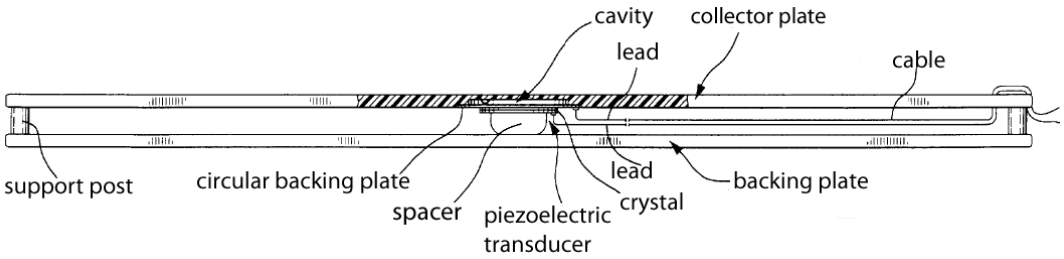


Figure 17: Improved Angelcare sensor mat design

In the third Angelcare patent (Pinsonneault et al, 2001), the new improvement does not relate directly to the piezoelectric sensor configuration, but to the mechanism by which the upper and lower plates can move relative to each other. They are connected together via sliding vertical connector pins with lateral projections to allow essentially friction-free movement between the plates, when the plates are at a predetermined distance apart. This makes the movement detection more efficient, due to the reduction of friction.

Figure 18 below shows an example of an Angelcare baby monitoring system currently on the market. The system includes a remote monitor and audio intercom, to allow parents to monitor the baby from another room.

Figure 18: A currently available Angelcare baby monitoring system

4.4 The Babysense II monitor, by Hisense Ltd

In May 1992, soon after the original Angelcare system became available, but prior to the later two Angelcare developments, an Israeli company, Hisense Ltd, filed a patent (Shtalryd et al, 1992) for an alternative design of piezoelectric movement sensor mat. The structure of the Hisense mat is shown in figure 19 below.

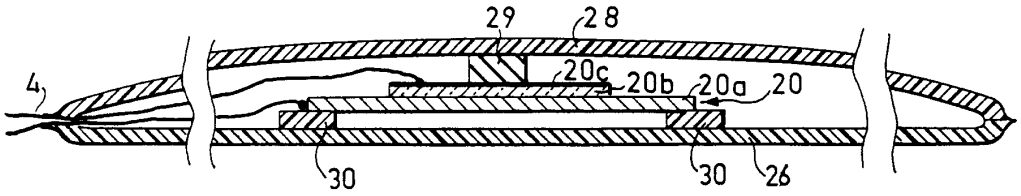


Figure 19: The Hisense pressure sensor mat design

The Hisense mat has an annular spacer ring (30) attached to the interior side of the rigid plate forming its lower surface. An electrode is attached across the annular spacer ring, and the upper side of the electrode is fixed to the piezoelectric crystal. A spacer is provided above the piezoelectric crystal, and adjacent an upper force collector plate. Any pressure on this upper plate is transmitted through the spacer, causing the piezoelectric crystal to bend and the lower electrode to bend inside the annular ring. This creates a more sensitive detector than the original Angelcare design. The Hisense mat is thicker than the Angelcare mat, due to the need to incorporate the annular ring inside the mat. The signal processing electronics is fairly similar to that used in the Angelcare products, and a block diagram is shown in figure 20 below. The signal from the movement detector is filtered, amplified and sent to a controller. Detection of the absence of breathing causes the controller to activate various alarms, although not all of these alarms may be needed.

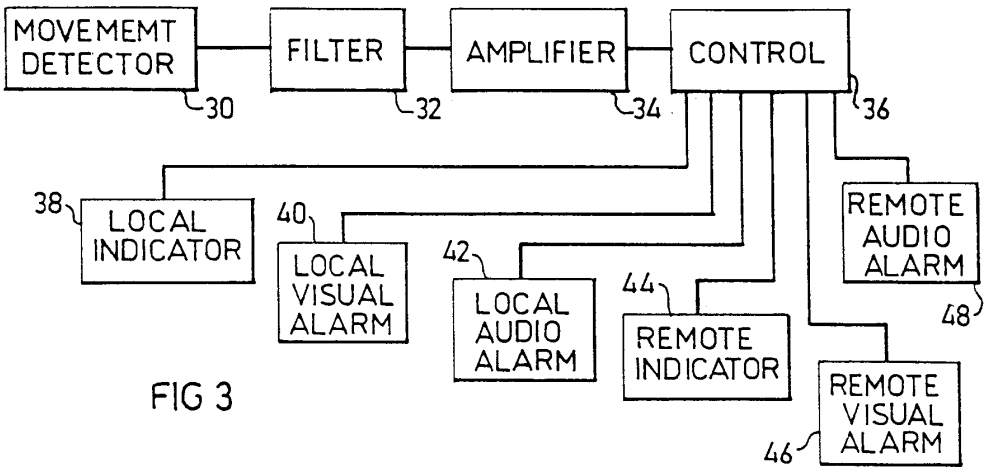


Figure 20: Block diagram of signal processing electronics in the Hisense detector

The Hisense design is currently used in their Babysense II product, which is shown in figure 21 below. Further information about the Babysense II product is provided at http://www.babysense.net/About-Hisense.asp and the manufacturers specifications are shown in Appendix C of this thesis.

Figure 21: The Babysense II system, by Hisense

The Babysense II baby monitor kit includes two sensor mats, to allow a greater area of the cot to be monitored, e.g. for babies over 6 months old who are more mobile and can move about the cot, and can be used with a single mat or both mats.

The Hisense sensor mats plug into a battery operated control unit. LEDs are provided on the front of the controller to indicate power on, low battery and alarm. One of the LEDs flashes every time the unit detects a breathing movement. If no breathing movements are detected in a pre-determined time, then an audio alarm in the control unit is sounded. The control unit may be attached to the side of the baby's cot.

The Hisense mats have a CE mark, and are currently used in hospitals for monitoring premature and sickly babies and infants.

4.5 Other pressure sensitive piezoelectric mats

The original Angelcare patent by Millns (1986) has now expired, and a number of other companies are now manufacturing pressure sensor mats which appear to be similar to the original Millns design. A number of additional brands of pressure sensitive baby monitor mat are now appearing on the market, as discussed below.

4.5.1 The Sensorium APN-1 apnea monitor

The APN-1 Apnea Monitor, by Sensorium (www.sensorium.co.uk) is shown in figure 22 below. No technical information could be found on the internal structure of the mat, although it appears to be similar in dimensions to the original Angelcare design. No sensor mat patents could be found for Sensorium. Note that the name "Apnea" monitor does not suggest that the device is being used for monitoring of sleep apnea. Apnea refers merely to lack of breath, and this type of monitor is designed to detect isolated breathing cessations in babies and infants.

Figure 22: The APN-1 Sensorium sensor mat

4.5.2 The Tommee Tippee baby sensor mats

Tommee Tippee is a part of the Mayborn Group Limited (www.mayborngroup.com) and further information on the Tommee Tippee mats is provided at http://www.tommeetippee.co.uk/product/digital_monitor_sensor_pad/

Tommee Tippee sells a wide range of baby products, in addition to several baby mat monitor products. The Tommee Tippee monitor systems include the "Closer to Nature" Sensor Mat Monitor and the "Suresound Ultimate Monitor". An example of the "Closer to Nature" system is shown in figure 23 below.

Figure 23: The Tommee Tippee Closer to Nature sensor mat system

No Tommee Tippee patents could be found relating to pressure sensitive mats. However, Tommee Tippee does hold patents relating to the automatic channel selection (ACS) feature of the audio link that is used in their baby sensor systems. In customer feedback reviews on websites such as amazon.co.uk, the Tommee Tippee mats appear to achieve generally poorer customer reviews than the Angelcare mats or Hisense mats. The Tommee Tippee systems are not CE approved and are not considered as medical devices.

4.5.3 The Nanny BM-02 breathing monitor

Nanny Monitor (UK) Ltd is UK distributor for Jablotron, a Czech alarm systems manufacturer. The Nanny sensor pads are the largest on the market at Sensor mat at

350 mm x 550 mm x 15 mm, and Nanny claims that they are 40% larger than the next biggest. Like Hisense, it is possible to use two sensor mats at the same time to cover a larger area. The Nanny mats have a CE mark. More information is provided at http://www.nannymonitor.co.uk/ and at http://www.babymonitor.co.uk/pages/fullProd.php/NANNY_BREATHING_MONITOR/23 . A picture of the mats is shown in figure 24 below.

Figure 24: The Nanny baby monitor mat

4.5.4 The Johnson & Johnson "intouch" monitor

A picture of the Johnson & Johnson device is shown in figure 25 below, and more information is provided at:
http://www.babyworld.co.uk/information/products/product_tests/monitors/monitors_full.asp

Figure 25: The Johnson & Johnson intouch monitor

No Johnson & Johnson patents could be identified for these mats. Further general information on baby breathing monitors is provided at the following website: http://www.anawiz.com/acatalog/Breathing_Monitors.html

4.5.5 The Tomy Movement Sensor Pad monitor

Tomy are a completely different company than Tommee Tippee, discussed above. The Tomy Movement Sensor Pad monitor is shown in figure 26. It constantly monitors movement with an audible soft click and a light indicator. An alarm is sounded if the baby stops moving for a period of 20 seconds.

Figure 26: The Tomy baby sensor mat

More details are provided at:
http://www.anawiz.com/acatalog/Tomy_Movement_Sensor_Pad_Monitor.html

4.6 Summary and conclusions

In summary, there are a range of pressure sensitive mats on the market, but these are targeted at baby monitoring, both in a home and a hospital environment. Reportedly, some of these sensor mats have a high rate of false alarms. As a result, these monitors may actually create more anxiety than provide peace of mind for some parents.

A question to ask is why have these pressure sensitive piezoelectric sensors not previously been used with adults, in the detection and monitoring of sleep apnea? Although these devices are sometimes described as "apnea monitors", where apnea means "lack of breathe", this does not suggest that they were intended for the

monitoring of sleep apnea syndrome, in which cessation of breathing is a frequent and temporary occurrence. In fact, sudden infant death syndrome (SIDS), also known as cot death, was much more of a concern. The baby monitors are configured to respond by sounding an alarm if the baby's breathing movements cease, to alert parents or hospital staff. However, this would be counterproductive to a patient with sleep apnea because the alarm would constantly be wakening them. A long series of repeated awakenings is exactly what needs to be prevented in sleep apnea patients. A sleep apnea patient may have hundreds of apnea episodes in a single night, potentially setting off the alarm hundreds of times. For babies, on the other hand, activation and sounding of the alarm was expected to be the exception, rather than the rule.

Also, for babies, a key advantage of the pressure sensitive mat is that no physical contact at all is required between the baby and the detector. This is less of an issue for adult patients in a hospital environment where they are being monitored constantly by medical staff. There were some concerns that the baby sensor mats would not be as reliable under a thicker mattress, even if they worked well under a thin cot mattress. For sleep apnea patients, alternative types of sleep apnea detection apparatus were more established and more accurate, albeit that they were not suitable for real-time detection and/or not sufficiently comfortable for long term regular use.

Possible methods of improving the sensitivity of these piezoelectric sensor mats include refinement and improvement of the breath sensing algorithms used. The basic design uses simple analogue filtering, and this may be susceptible to interference from mains electricity, radiofrequency signals, and other sources. Thus, the use of digital signal processing techniques may produce "cleaner" results with fewer false alarms. Also, for sleep apnea detection, there could be benefits to using the sensor mats together with one or more additional signal sources, e.g. a microphone for monitoring breathing sounds, or a chest belt for monitoring breathing movements. The combination of different types of sensors could provide a higher accuracy than a single type of sensor alone. Part of the aim of this thesis is to

evaluate whether the sensor mats appear to have a high enough sensitivity and accuracy when used alone.

The following chapters review current treatment methods and possible means of interrupting sleep apnea episodes, which will be necessary for a new sleep apnea detection and interruption system.

5. Current Methods of Treating Sleep Apnea

A number of different methods are currently used to treat sleep apnea, and these are reviewed below.

5.1 Behavioural therapy

Behavioural therapy or lifestyle change is often adopted in parallel with other types of therapy. In mild cases of sleep apnea, such changes may be sufficient to cure or substantially reduce the problem (Sanchez et al 2009). However, alone, it is insufficient to resolve the problem in many patients.

Obesity or being overweight is a well known risk factor for OSA (Dement 2000). It was originally believed that sleep apnea symptoms were always related to obesity, in a condition known as "Pickwickian syndrome", named after an obese and very sleepy character Joe in the novel "The Posthumous Papers of the Pickwick Club" by Charles Dickens. About 90% of people suffering from Pickwickian Syndrome (now also known as Obesity hypoventilation syndrome) do in fact have sleep apnea (Mokhlesi & Tulaimat 2007), although the converse is not true. Weight loss can be very helpful for some patients. However, only 50% of sleep apnea patients are obese (Mortimore et al 1998), and many sleep apnea sufferers are not actually overweight. In fact, general obesity is less of a risk factor for sleep apnea than a high fat distribution around the neck area (Dancey et al 2003). This neck fat distribution reduces the airway diameter, and also causes increased loading on the airway. Men tend to be more susceptible, as they tend to accumulate fat on their upper body, but women tend to accumulate fat more on the hip and thigh area. It is also thought that pre-menopausal women may be protected to some extent by hormonal factors which influence upper airway dilator activity.

Redolfi et al (2009a) has found that even in non-obese men, fluid displacement from the legs into the neck reduces the upper airway size and increases its collapsibility. Sitting for prolonged periods of time can lead to fluid accumulation in the legs. When the person lies down in bed, the pressure on the legs reduces, resulting in fluid moving upwards in the body. This effect was not observed in women (Redolfi

2009b). In Redolfi's more recent research (as reported in Rattue 2011), wearing compression stockings such as flight socks during the day was found to reduce fluid retention in the legs, and also to reduce the severity of sleep apnea in patients with chronic venous insufficiency (e.g. resulting from heart failure or hypertension), where sufficient blood was not being pumped from the veins back to the heart. The increase in neck diameter at night due to fluid movement was measured, and found to correlate with the number of apneas/hypopneas per hour. Redolfi also discusses the fact that OSA is more prevalent in patients with edematous states, such as heart and renal failure, than in the general population, despite lower body weight, and this further supports the possibility that fluid retention may increase the risk of OSA (Redolfi 2009a).

Having the patient sleeping on their side instead of on their back may prevent the tongue and palate falling backwards to block the airway, and it may also increase the oxygen storage in the lungs, therefore also having a beneficial effect for central sleep apnea patients. Special items of clothing have been developed to discourage sleeping on the back. A similar approach is to put a tennis ball or golf ball into a sewn pocket on the back of a T-shirt, worn in bed at night, so that the sleep apnea patient will find it uncomfortable to lie on their back and will quickly move to a different sleeping position.

Oropharyngeal exercises may be useful for some patients, to strengthen the muscles around the airway. A set of exercises was devised by a Dr Flack in 1960, and was found to be safe and also to be effective for a number of patients (Lipman 1990). Learning to play the didgeridoo can help reduce snoring and sleep apnea, apparently by strengthening muscles in the upper airway so that they are less likely to collapse while the patient is asleep (Puhan 2005).

Alcohol and sleeping pills can relax the muscles in the throat, and avoiding these can result in much better quality sleep and reduced risk of sleep apnea. Smoking irritates the tissues of the throat region, causing excess mucus production and narrowing the airway. Smoking also increases the risk of heart attacks and strokes, and reduces the

ability of the blood to carry oxygen. Thus, patients who stop smoking may improve their sleep apnea symptoms.

5.2 Continuous positive airway pressure (CPAP)

Continuous positive airway pressure (CPAP) was first used in 1981, and is currently the most successful treatment method for sleep apnea, and is suitable for moderate to severe sleep apnea. The patient wears a pressurized mask during sleep to keep their airway open, preventing collapse of the windpipe and making it easier to breath. The pressurised air is generated by a flow generator, and delivered through a flexible tube to a nasal mask. More advanced CPAP machines may monitor the patient's breathing. CPAP is safe and is effective for many patients.

For patients who sleep with their mouth open, a full face mask may be necessary for their CPAP treatment, and an example of this is shown in figure 27 below. Patients breathing through their nose may use a nasal CPAP machine. It may be possible to encourage nose breathing using a strap to keep the jaw closed during sleep, although this may be uncomfortable.

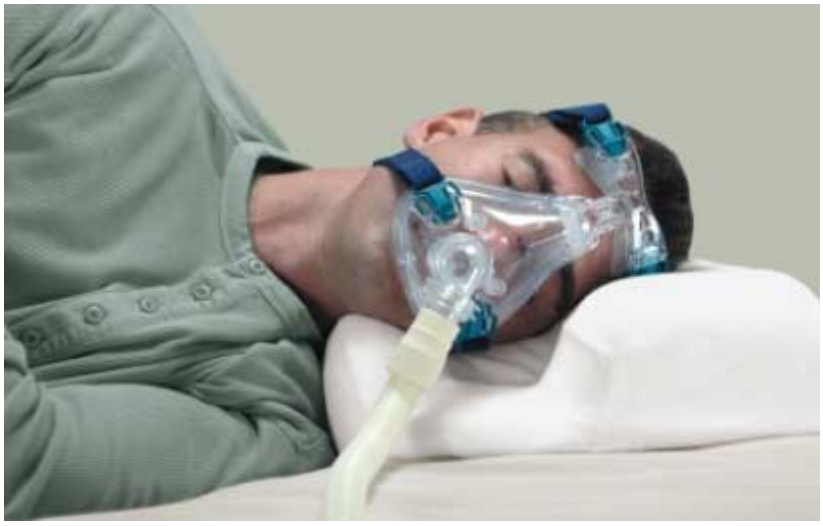


Figure 27: A patient wearing a CPAP device with a full face mask

CPAP can significantly raise average blood oxygen during sleep, and the effectiveness of CPAP is discussed by Loredo et al (1999). Randomised controlled trials, comparing CPAP with placebo CPAP, show that CPAP reduces the number of

micro-arousals, increases oxygen saturation, and improves the AHI for many sleep apnea patients, without any change in total sleep time, sleep onset time, or the time spent in each sleep stage. Infection or other major side effects are rare with CPAP. Also, Duran-Cantolla (2009) found, on review of a number of studies, that CPAP results in a reduction of blood pressure of about 2 mm Hg. This is considered to be beneficial for reduction of both cardiovascular and cerebrovascular risk.

However, CPAP is not successful for all patients. A high proportion of patients trying CPAP will show poor compliance and/or will refuse the treatment. According to Walsh et al (2011), in studies using an adherence criterion of at least 4 hours per night, adherence rates are frequently less than 50% of CPAP users. CPAP is uncomfortable to wear and use, as discussed by Terrier (2003), and many patients can't tolerate the way the mask feels on their face. Nasal CPAP devices may be more comfortable, but are unsuitable for use by mouth breathers. Particularly with nasal CPAP machines, if a patient has problems with congestion and symptoms of the common cold, they may be unable to use CPAP.

CPAP masks tend to come in a limited range of standard sizes, and may be poorly fitting on a high proportion of patients, resulting in skin breakdown and air leakage. This occurs in about 50% of patients. The patient may experience nasal and mouth dryness and congestion from the use of CPAP. This can be improved by incorporating a humidifier into the CPAP device to humidify the delivered air. However, even this may not be satisfactory, as the correct humidity setting may vary with environmental factors, and may need to be continually adjusted. Having it set too high is also uncomfortable for the patient, and can result in water running down their nose, which may waken them.

The constant noise from the CPAP machine may be a problem for both the patient and their bed partner. Also, if the CPAP pressure is particularly high, it can cause side effects such as ear and chest discomfort, reduced cardiac output and renal function, and the AHI may actually increase in CSA patients.

CPAP is not a cure for sleep apnea, but merely provides a "pneumatic splint", in the form of a pressurised air flow, to keep the airway open while a person is asleep. The symptoms of sleep apnea will return immediately if a patient stops using CPAP.

CPAP is not recommended for patients with certain other medical complications, e.g. where anatomical abnormalities prevent an upper airway seal or patients with floppy epiglottis with a risk of prolapse. In patients with mixed sleep apnea, the positive pressure may eliminate the obstructive component of the sleep apnea, but the central sleep apnea component may persist during the CPAP treatment.

Bi-level Positive Airway Pressure (Bi PAP) is similar to CPAP, except that the inspiratory and expiratory pressures are independently adjusted. It appears to have no significant advantage over standard CPAP in straightforward cases of OSA, but it could be more useful for patients with respiratory failure.

Autotitration (AUTO CPAP) involves the "smart" adjustment of the pressure, so that it is lower when a patient is awake, thus reducing some of the nasal side effects of CPAP. AUTO CPAP is more expensive than standard CPAP, so even though it may be more comfortable, it is generally only used in cases where there is a problem with standard CPAP.

5.3 The PROVENT nasal device

The PROVENT nasal device (http://www.proventtherapy.com), as shown in figure 28, is a new device that provides an alternative to CPAP for some patients. It fits over the patient's nostrils, and using a proprietary micro-valve, it generates a positive pressure in the airway by means of the patient's own breathing, to keep the airway open without the need for a mask or a machine. During an inhalation, the airflow is nearly unobstructed, so that the patient can breathe normally. During exhalation, the micro-valve closes and air is directed through small air channels, increasing the resistance, and creating EPAP (Expiratory Positive Airway Pressure). This keeps the airway propped open until the patient inhales again. The PROVENT device is FDA-approved for OSA treatment, and is available on prescription only. It can be used

with mild, moderate and severe OSA. As discussed by Walsh et al (2011), the PROVENT device looks promising although it may take time for patients to get used to using it.

Figure 28: The PROVENT nasal device

5.4 Dental appliances and intra-oral devices (IODs)

Physical intervention by means of dental appliances and intra-oral devices (IODs) may be directed to the nasal passage, throat (pharynx), base of tongue, facial skeleton, or a combination of these. The most popular of such techniques is mandibular advancement, which involves causing an anterior displacement of the mandible, to produce more space in the upper airway. Mandibular advancement has been found helpful for 50% of mild to moderate OSA cases. However, side effects may include hypersalivation and gum and teeth discomfort, especially at first.

5.5 Surgical methods

Various surgical approaches are described below, and these have been successful in some patients. However, the surgical approach carries a risk of infection and complications, and it is not successful or helpful in all patients. For these reasons, it is adopted as a last resort solution for seriously affected patients. Surgery on the mouth and throat can cause postoperative swelling of the lining of the mouth and other areas that affect the airway. Even when the surgical procedure is designed to improve the airway, such as tonsillectomy and adenoidectomy or tongue reduction, swelling may negate some of the effects in the immediate postoperative period. Once the swelling resolves, the full benefit of the surgery may be noticed.

5.5.1 Tracheostomy

The first successful surgical technique to be used for sleep apnea was tracheostomy, which involves making a hole in the trachea to allow air to enter (Dement 2000). The hole could be closed during the day using a stopper, and opened at night to facilitate breathing. This was successful for simple cases of sleep apnea, though often less beneficial in more complex cases. However, it has a risk of infection, scarring, inflammation and damage to speech. Today, tracheostomy is used today only as a last resort, as much better options are now available instead.

5.5.2 Uvulopalatopharyngoplasty

Uvulopalatopharyngoplasty (UPPP) is a surgical reduction of the uvula, tonsils and/or some of the soft palate, to increase the space in the upper airway. Treatment is often performed using a laser, and this is known as LAUP. Side effects may include changes in voice pattern and worsening of gastrooesophageal reflex disease (Kezirian et al, 2006). Tonsillectomy is also an option to reduce obstruction in the pharynx.

5.5.3 Maxillomandibular advancement

Maxillomandibular advancement (MMA) is considered to be one of the most effective surgical techniques for sleep apnea patients. It increases the posterior airway space, reducing the chance of airway collapse. A meta-analysis by Holty & Guilleminault (2010) showed that the mean apnea–hypopnea index (AHI) decreased from 63.9 episodes per hour to 9.5 episodes per hour ($p < 0.001$) following MMA surgery. The overall risks of MMA surgery are considered to be low, and Guilleminault's study found only 4 failures out of a series of 177 patients (around 2%).

5.5.4 Transpalatal advancement pharyngoplasty (TAP)

Transpalatal advancement pharyngoplasty (TAP) is the latest type of surgery that may be beneficial to sleep apnea patients. It aims to reduce or prevent the airway obstruction by creating a larger space in the area behind the roof of the mouth. According to Shine & Lewis (2009), for 60 patients who had TAP surgery for sleep

apnea between 2002 and 2006, an improvement in the apnea/hypopnea index (AHI) and blood oxygen saturation was seen in 38 patients (63%), and 21 patients (35%) were completely cured of sleep apnea.

5.5.5 The Pillar Procedure

The Pillar Procedure is a minimally invasive treatment to reduce snoring and obstructive sleep apnea, by increasing the stiffness of the soft palate. In an operation that usually takes no more than half an hour, three to six Dacron strips are inserted into the soft palate using a modified syringe and a local anaesthetic. The effect is to reduce vibration or collapse of the soft palate. The procedure has been helpful for some patients, but if collapse of the tongue or narrowing of the nasal airway are also present during the sleep apnea, then the Pillar Procedure alone is unlikely to be sufficient and additional treatments would also be needed.

5.5.6 Hypoglossal nerve stimulation

Many attempts have been made to electrically stimulate the hypoglossal nerve and the genioglossus muscle. The hypoglossal nerve stimulates the muscles of the tongue and upper airway. The hypoglossal (XII) nerves are anatomically deep seated, which makes them relatively difficult to stimulate. As a result, many studies have used an implantable electrode (e.g. Oliven et al, 2003), and with a programmable pacemaker (Penzel et al, 2001), and it has been found to have beneficial effects. However, in another study it was found that the amplitude had to be increased after 6 months, and the effectiveness was very dependent on body position and sleep stage. Guilleminault et al (1995) found that electrical stimulation is only effective if it is generating alpha-wave EEG arousals, and that it may act on unnecessary muscles as well as the targeted muscles. Kezirian (2010) discusses research on upper airway neuromuscular electrical stimulation in animals and humans, including results from eight obstructive sleep apnea patients with a fully implanted system for hypoglossal nerve stimulation, demonstrating an improvement in upper airway collapsibility and obstructive sleep apnea severity.

In December 2010, Inspire Medical went into clinical trials for their implantable device. The Inspire implantable system is shown in figure 29 below. The system includes a device that is implanted in the chest, with a stimulation lead passing under the skin to the hypoglossal nerve in the neck. The battery has a life span of 3 to 5 years.

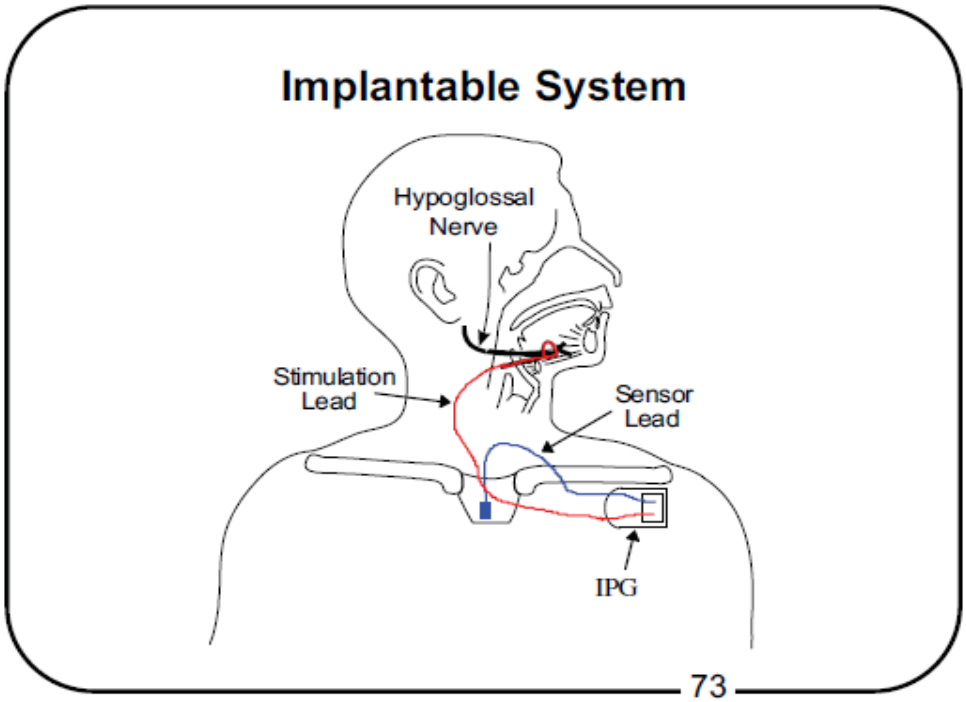


Figure 29: The Inspire™ I implantable nerve stimulation system (Kezirian et al 2010)

Another company, Apnex Medical of St. Paul, Minnesota is conducting a clinical trial of a competing product, the Apnex Hypoglossal Nerve Stimulation (HGNS™) System.

It would be preferable if it was possible to stimulate the hypoglossal nerve without an implant, and one other approach is transcranial magnetic stimulation (TMS). Lo and Fook-Chong (2006) evaluate the use of a double cone coil in eliciting tongue responses at the posterior head region. They were able to achieve activation at or distal to the hypoglossal nuclear level, but proximal to the hypoglossal canal region. This contrasts with earlier studies on TMS of the parieto-occipital region using a round coil, which had difficulties in eliciting tongue motor responses.

Future research is ongoing in hypoglossal nerve stimulation, and it is likely that further optimization of device features and stimulation parameters will be seen. Patient selection may also be an important issue. Eventually, hypoglossal nerve stimulation may be regarded as a viable alternative to positive airway pressure therapy.

5.5.7 Summary for surgical treatments

In addition to the surgical techniques discussed above, various other surgical procedures are available, including hyoid bone myotomy and suspension and various radiofrequency technologies. Weaver (2010) reviews the success of different surgical techniques, and recommends that Maxillomandibular Advancement should be available to patients, and hypoglossal nerve stimulation should be developed. Various other surgical therapies may be considered in specific cases, because they can provide important clinical benefits.

5.6 Medication

Drugs may be prescribed to open the nasal passageway, to stimulate respiration, to promote wakefulness during the day, and/or to inhibit REM sleep (Lipman 1990). Only a small number of medications have been found to be effective for obstructive sleep apnea - these are protriptyline, fluoxetine, theophylline and progesterone. Acetozolamide and theophylline have been used for central sleep apnea - acetozolamide is believed to work by lowering blood pH and encouraging respiration. Another possibility is to use a nocturnal oxygen supply, but this could be inadvisable for patients with high blood carbon dioxide levels.

The use of sedatives, analgesics and anaesthesia (e.g. during surgery) may cause serious life-threatening risks to sleep apnea sufferers, because they may cause life-threatening breathing irregularities or airway collapse.

5.7 Conclusion

Many of the above sleep apnea treatments have provided considerable benefits to many patients. However, each has its own disadvantages, and none are suitable for all patients. It is desirable to continue the search for new and improved methods of sleep apnea treatment and prevention.

6. Devices for Interruption of Sleep Apnea Episodes

Chapter 5 discussed current treatment options for sleep apnea. The most successful treatments were CPAP, lifestyle changes, and certain types of surgery. However, CPAP is uncomfortable and inconvenient and not all patients will benefit from lifestyle changes or surgery. In fact, for some patients, there is no currently available effective treatment, as they cannot tolerate CPAP or do not find it to be helpful, they do not find lifestyle changes to be sufficiently helpful, and for various reasons, they are not regarded as suitable candidates for surgery. New treatment options are urgently needed to help such patients.

This chapter considers possible methods of interrupting and stopping a sleep apnea episode after detection of its commencement, and restarting the patient's breathing. The aim is to re-start the breathing without the patient actually being awakened. In some patients, this may not be possible by non-invasive means, e.g. as their sleep apnea may be too severe. Some such patients may also have daytime breathing difficulties. However, in other patients, particular those with milder sleep apnea or those who experience sleep apnea episodes only in certain sleeping positions, such an approach could be very beneficial.

A successful device would detect sleep apnea and interrupt it before the blood oxygen levels drop significantly, and before either the oxygen drop or the increased respiratory effort (in the case of OSA) led to the patient being awakened. To obtain a beneficial effect, it may not actually be necessary for such a device to stop sleep apnea 100% of the time, and even with, e.g. an 80% successful intervention rate, the number of harmful apnea episodes would be greatly reduced, and the overall health of the patient may improve significantly.

It is a challenging problem to disturb the patient sufficiently to interrupt the sleep apnea without actually awakening them in the process. However, anecdotal evidence suggests that this may be possible. For example, it has been reported by the wife of a sleep apnea patient that gently tickling her husband on the abdomen can bring him out of the sleep apnea and start him breathing again (Terrier, 2003). It is worth also

considering techniques and devices for stopping a person snoring, because interruption or prevention of snoring can also involve changing the person's breathing pattern. Various comments posted on a number of online forums give suggestions on how to stop someone snoring, and these are summarised below:

- Giving someone a nudge. If a gentle nudge is insufficient, then a shove or a push or an elbow to the ribs to get them to roll over and stop snoring.
- Poking them until they roll over onto their side.
- Nudging them or lifting their pillow a tiny bit. Sometimes they roll over, sometimes not.
- Pinching their nose to semi-wake them, and they will probably roll over to their side or stomach.
- Using my hair to tickle his nose or ear. He always rolls over and the snoring stops.
- Pressing down on the mattress and sighing loudly, to waken them enough to stop snoring.
- Telling them to turn over (maybe it won't wake them up)

These approaches appear to work by (1) getting the person to move into a different sleeping position, or (2) disturbing them enough to semi-awakening them. Although (2) may sound undesirable for sleep apnea patients, if done early enough, it may reduce long term health damage caused by hypoxemia and hypercapnia. Whether or not it is useful in practice may depend on how strong the arousals are, and how frequently they occur. A treatment that does not waken the patient most of the time, but does waken them occasionally, may still be very useful for some patients.

The above techniques can be summarised as nudging, tickling, poking, pinching, shoving, pushing, moving the pillow or mattress, and communicating by speech or sounds. In a practical device, it is highly undesirable to use a rough technique similar to pushing, shoving or elbowing, as that would be painful and uncomfortable to the patient, and could leave bruising and marks.

So, the question is which interruption methods are most effective and practical, without wakening the patient constantly? The following sections discuss various options in current use, for snoring or sleep apnea prevention.

6.1 Use of a vibrating actuator

The use of mechanical vibration is one of the simplest options, and the mechanical vibration is simply meant to replace the "nudge" or "tickle" discussed above.

6.1.1 The "Snoring U" iPhone app

Smartphones are increasingly being adopted for all sorts of purposes, and medical/health applications are no exception. "Snoring U" is an iPhone and iPad app that is intended to monitor and interrupt snoring. It is available from Pointer Software Systems, Ltd, via the Apple iTunes store.

Snoring U was developed under the guidance of Dr. Naveh Tov, MD, PhD, an Israeli physician specializing in internal pulmonary and sleep medicine. It does not claim to be a complete cure for snoring, but it does claim that it may help to stop individual snoring episodes. It provides feedback on snoring volume and duration, by recording and storing snoring sound data.

The software detects snoring sounds using the iPhone microphone. The user can pre-select how the iPhone responses to the snoring sound. One option is for Snoring U to deliver a small "nudge", i.e. a vibration or a pre-selected sound or both, to try and stop the person snoring. The volume of the sound and the maximum number of nudges per snoring event can also be set. Alternatively, it is not essential to use nudges at all, and the software can simply record the sound for later playback and analysis. A summary screen is provided to show total sleep time, snoring duration, snoring loudness and number of nudges received. A graph display is also provided, and the data can be uploaded to a computer. This can allow the person (and their doctor) to see how often they snore, and whether the nudges are helpful, as well as monitoring the progress over time.

A selection of screenshots from the "Snoring U" app is shown in figure 30 below, including the monitor screens, graphs and data lists.

Figure 30: Screenshots from the "Snoring U" app for iPhone and iPad

It is not clear how well the "Snoring U" app works in practice, but the average customer rating in the online Apple Store from 46 customers was only 2.5 stars out of 5. This suggests that it may have some value, but it is far from a complete cure for snoring.

6.1.2 The Respisense Ditto system

The Respisense™ Ditto Infant Tummy Movement Monitor is a baby breathing monitor and stimulator that has been on the market since 2005 (www.respisense.co.uk). It is a battery operated device that clips onto the waistband

of the baby's nappy to monitor the baby's abdominal movements. A picture of the device is shown in figure 31 below.

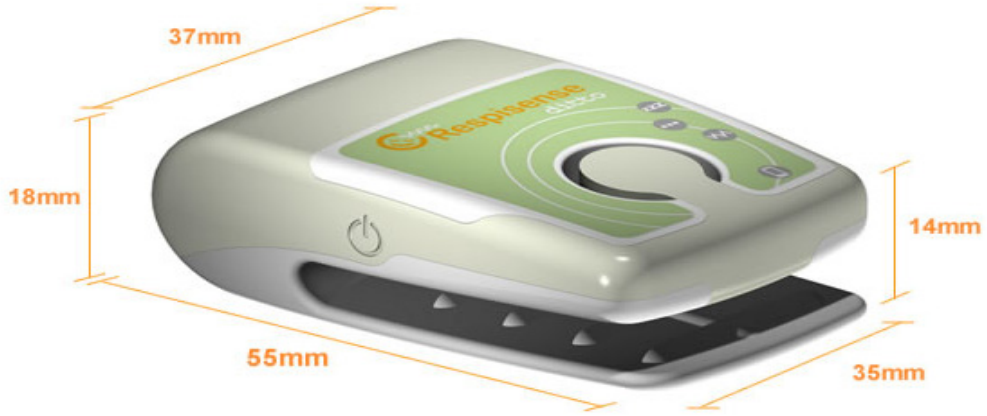


Figure 31: The Respisense Ditto Infant Tummy Movement Monitor

If no abdominal movements are detected from the baby after a 15 second inactivity period, a tactile stimulator is activated. This attempts to gently wake up the baby by stimulating its abdomen. If the baby's abdominal movements do not resume within 5 seconds of this stimulation starting, an alarm will sound to alert parents or carers to the potential danger. The alarm itself will usually stir the baby back to normal breathing activity. The device is configured to differentiate between rhythmic or general movements. It also allows sensitivity configuration, to reduce risk of too many false alarms. The Respisense Ditto monitor is intended to be used not just in the baby's cot, like the baby movement monitors previously discussed in chapter 4, but instead, it could be used practically anywhere that the baby may fall asleep.

6.2 Devices for electrical stimulation

Another approach to "disturb" the patient without wakening them is to use electrical stimulation. As discussed in chapter 5, this can be done as a surgical implant to stimulate the hypoglossal nerve. Here, we are more interested in non-invasive forms of electrical stimulation.

6.2.1 Non-invasive hypoglossal nerve stimulation

Electrical stimulation of the soft palate was attempted by Mañanas et al (2003) to try and restore muscle tone and clear the blocked airway. The stimulation was found not

to waken the patient when a 3mA stimulus at approximately 10V was applied. A beneficial effect was observed in some, but not all, patients.

6.2.2 Transcutaneous electrical nerve stimulation (TENS)

TENS is a well-established method of transcutaneous electrical nerve stimulation, normally used for stopping pain. However, due to the fact that the hypoglossal nerve is located deeply beneath the skin, there is no current evidence that TENS could be adapted as a sleep apnea treatment.

6.2.3 The "Snore Stopper" device

The "Snore Stopper" (as described in Lipman 1990) is a wristwatch type device including a microphone for detecting snoring sounds. On each detected loud snore, it gives the sleeper a mild electric shock that is not quite strong enough to waken them. The idea is to use conditioning to "train" the patient's responses by creating an association between snoring and electrical shock.

The photograph in figure 32 below shows the Silent Night Snore Stopper, sold on amazon.co.uk.

Figure 32: The Silent Night Snore Stopper device

This snore stopper is described as detecting snoring sounds, and then sending a weak electrical impulse to the wrist. The snorer feels these impulses and changes his sleeping position, without waking up and stops snoring. The intensity setting can be adjusted prior to use. The device is battery operated, and contact gel is used to ensure good electrical conduction to the skin. The average customer review from 7 customers on amazon.co.uk was 2 stars out of 5, and the details of the reviews suggests that it does work for some people some of the time, but it doesn't work for everyone.

Several alternative brands of Snore Stopper device are also available. The Lifemax Relax Snore Stopper received a rating of 5 stars out of 5 on amazon.co.uk from the single customer who had reviewed it. Instead of wearing it around his wrist, he reports attaching it to a longer elastic strap and wearing it on the front of his neck. He reported that it wakens him up if he starts snoring. A further brand, the Relax Snore Stopper, received a 4 star rating and a 1 star rating from two customers on amazon.co.uk. The 4 star customer reported that it worked well for him, preventing him from snoring without actually wakening him, and he reported getting a good night's sleep while using it, contrary to his expectations.

6.3 Stimulation by audible sound

The "Snoring U" app discussed above includes this option. However, the difficulty is that this type of stimulation may be too unreliable. For example, even the loud sound made by an alarm clock and intended to waken a person may be very variable in its effect. Sometimes, the person will waken before the alarm sounds or just as it starts, but other times, the person may sleep through a minute or more of the alarm sounding, or even sleep through it completely. Further investigation and testing would be needed to assess whether audio stimulation has any potential usefulness in sleep apnea treatment. A considerable disadvantage is that audio stimulation may waken the patient's bed partner in addition to disturbing the patient themselves.

7. A New Device to Detect and Interrupt Sleep Apnea

This thesis is concerned with practical and useful real-time methods of detecting sleep apnea and bringing the patient out of the apnea episode. One aim is to use a pressure sensitive mat to detect sleep apnea. This has the advantage of being completely non-invasive, as it makes no contact with the patient and imposes no restriction on their movements during sleep. Another aim is to find a suitable device and configuration for interrupting sleep apnea episodes without wakening the person. Each of these is discussed in turn below, followed by a discussion on a complete sleep apnea monitoring and treatment device.

7.1 Detection of breathing signals using a pressure sensitive mat

7.1.1 Equipment and methods

The first stage was to obtain a suitable pressure sensitive mat for use in the sleep apnea detection device. Since the Babysense™ II baby monitor kit, manufactured by Hisense, was CE approved, used in hospitals and readily available to purchase, it was decided to obtain a Babysense™ II baby monitor kit and attempt to use the output signal from the Babysense mat.

After obtaining a Babysense™ II baby monitor kit, which included a controller and two pressure sensitive mats, one of the two mats was carefully opened to examine the interior. The photograph in figure 33 below shows the interior appearance and layout of the mat. The mat is made up of two interlocking rigid plastic plates. The plates have spring-loaded projections near the corners to resiliently bias the two plates away from each other when the mat is in use. Projections at the edges of the plates prevent them being separated apart by too great a distance. The mat contains no signal processing electronics, but only a standard piezoelectric element, similar to that found in a basic audio buzzer. The piezoelectric element is located in the centre of the mat, housed within a raised plastic ring. A projection on the opposite plate is located to press against the piezoelectric element when the mat is in use, so that any force applied to that plate is transmitted to the piezoelectric element.

Figure 33: Inside of a Babysense II pressure sensitive mat

An enlarged view of the piezoelectric element is shown in figure 34 below.

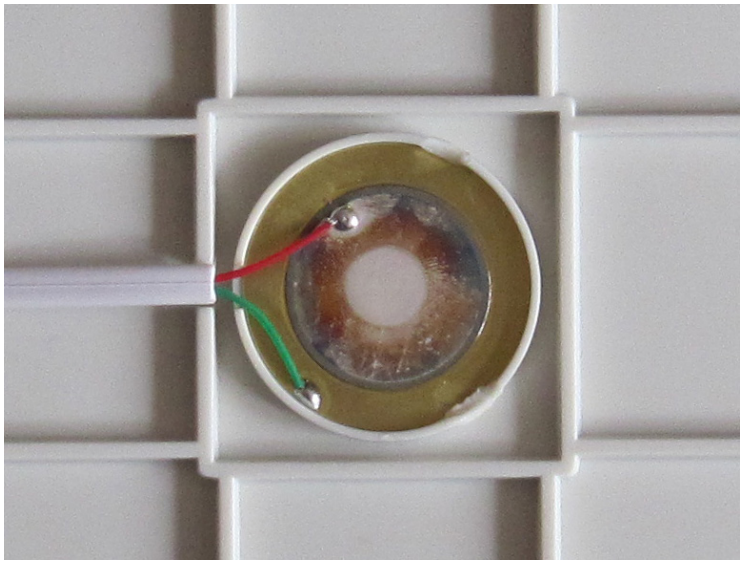


Figure 34: Enlarged view of the piezoelectric sensor in the Babysense II mat

Figure 35 shows the interior of the Babysense II control unit. The control unit includes a push button switch to allow the device to be switched on and off, and this is protected by a sliding cover on the outer casing to prevent the switch from being accidentally pressed. The unit has a red LED for indicating a low battery, another red LED which functions as an alarm indicator, and a green LED which flashes each time a breathing movement is detected. A speaker is provided to set off an audio

alarm at the same time as the alarm LED is activated. Two grey connectors (shown at the bottom of the photo) are RJ11 sockets, and either a single mat or two mats may be plugged into them when using the device. When both mats are connected, their input signals are combined in parallel.

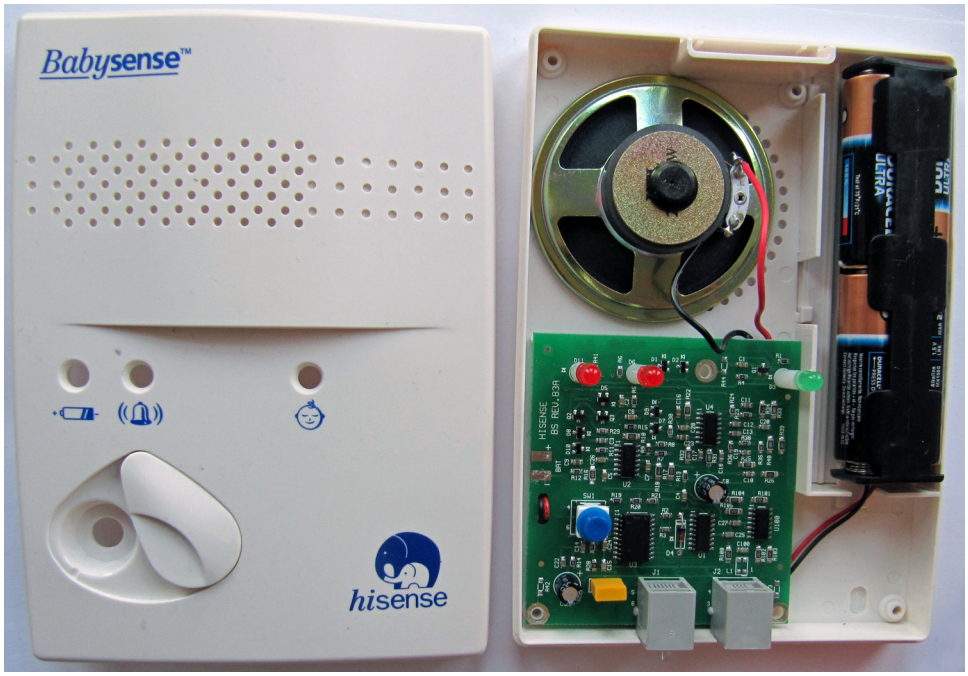


Figure 35: Interior of the Babysense II control unit

With a single mat connected to the Babysense controller, pressure was applied to the mat by hand at regular intervals of about once per 3 seconds. The green LED was observed to flash just after each application of pressure. On ceasing to apply pressure, the alarm would usually sound after 20 seconds and the alarm LED would light. However, sometimes, the device appeared susceptible to interference, as flashes of the green LED would occur for no apparent reason. Sometimes this did not affect the alarm timing, and the alarm would still sound after 20 seconds. However, other times, the alarm took longer than expected to sound. The controller has an automatic sensitivity adjustment mechanism, and possibly this was configured for optimal sensitivity with movements equivalent to a baby's breathing. The Babysense II mat was also tested under a mattress while attached to the Babysense controller. When lying on top of the mattress and breathing normally, the green LED would normally flash on each breathe. However, some interference was still seen at times.

For example, the LED sometimes flashed when no-one was lying on the mattress and no movement was occurring. It is not clear whether the interference is mainly affecting the controller or is also affecting the mat itself. If necessary, additional screening materials could be used within a sleep apnea detection device, to reduce interference. In the prototype device that is discussed below for sleep apnea detection, the Babysense controller is not used, and the Babysense pressure sensitive mat is used on its own.

The pressure sensitive mat had a cable attached to the piezoelectric sensor inside the mat at one end, and attached to an RJ11 plug at the other end. In order to access the output signal from the mat, an adaptor was constructed using an RJ11 socket and wires connected to the appropriate RJ11 pins. The other end of the wires were exposed to allow them to be plugged into a breadboard or attached to an oscilloscope probes. Insulating tape was applied around exposed parts of the adaptor to prevent any accidental short circuits or contact with other pins. The RJ11 plus on the mat's cable was inserted into the RJ11 socket of the adaptor.

Using a volt meter, the voltage levels from the mat were observed to rise as high as several tens of volts when pressure was applied to the mat. The voltage increased in response to an increase in the applied pressure, and then returned to zero when the pressure stabilised. If the load was then decreased, the voltage went negative in response to the change, and then stabilised back to zero. Thus, the mat does not detect the actual force applied, but instead it detects any change in applied force.

The voltage signal from the piezoelectric sensor was recorded to a computer using a Picoscope 2205 USB oscilloscope, set to a 1kHz sampling rate, and the Picolog data logging software. This allowed measurements to be recorded over a period of hours. More information on the Picoscope USB oscilloscope is provided in Appendix B.

The mat was placed under a large, thick cushion (equivalent to a thin mattress). Voltage data was recorded with the present author lying on top of the mat and breathing normally for a number of seconds, then holding the breath for about 30

seconds, before resuming normal breathing again. In order to try out different signal processing and filtering parameters, the data was imported into the MATLAB software package, and various different filter settings were tested. It was necessary to convert the data output of the Picolog software into a format suitable for importing into Matlab. Appendix F shows the computer code written by the present author for this purpose.

7.1.2 Results and discussion

The detected voltage was plotted against time, and is shown in figure 36 below as the red trace on the graph. It can be seen that the data is very noisy without filtering, and the noise includes heartbeats and 50Hz mains hum. The noise in the signal was very significantly reduced with the use of a 5th order low-pass Butterworth digital filter with a 0.5Hz cut-off frequency, and the filtered data is shown as the heavy black trace on the graph. This shows a clear breathing signal which levelled off during the breath-holding period and resumed when the breathing re-started. The breathing peaks and troughs can clearly be seen, at a rate of one cycle about every 5 seconds.

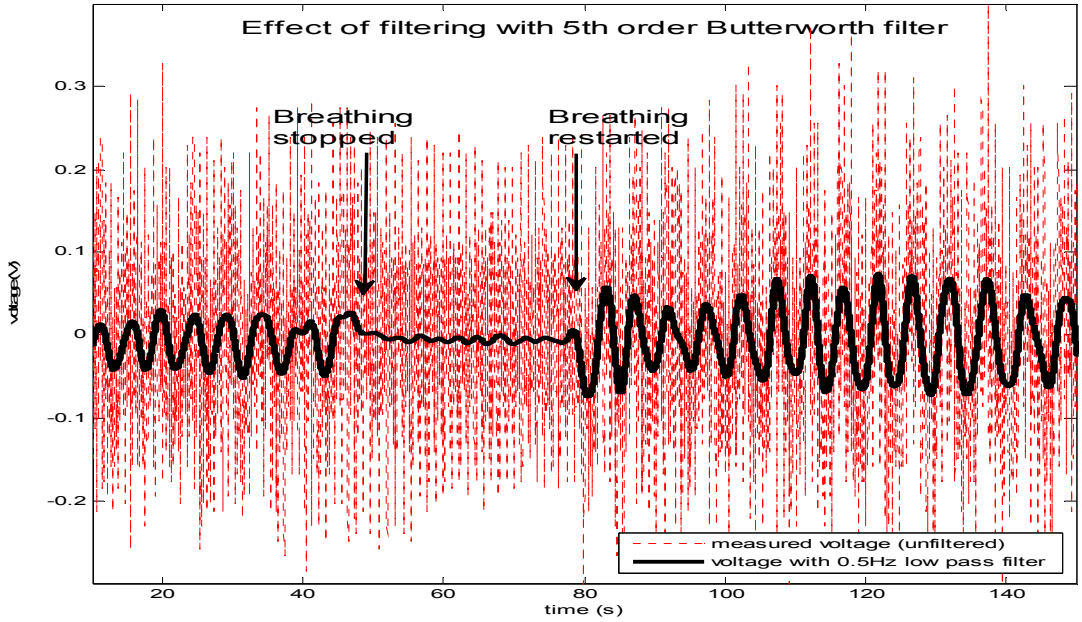


Figure 36: Graph of original and filtered pressure measurements from the mat

Although these results were not processed in real-time, it would be a straightforward matter to implement the selected algorithms in a real-time process, either on a computer or using dedicated signal processing hardware.

The procedure was repeated with the mat placed under a normal bed mattress, on top of a rigid wooden board on the bed base, to prevent uneven pressure due to the slats of the bed base. The voltage level corresponding to the breathing was lower, but the breathing signal could still be clearly identified, and any absence of breathing could be detected. The breathing signals had a clear sinusoidal form when lying directly above the mat, but a more distorted waveform after moving further away on top of the mattress.

No significantly strong interference signals were observed when there was no pressure on the mat. The use of digital signal filtering algorithms, rather than the analogue filtering as in the original baby monitors, may increase the quality and reliability of the breathing signal detection.

The situation of holding the breath and lying still is a method of simulating central sleep apnea (no breathing and no respiratory effort). A simple threshold algorithm (e.g. relative to a local average) applied to the filtered data may be sufficient to detect the beginning of a CSA episode. The breathing cessation should be at least 10 seconds long for an apnea episode. If the person moves during their sleep, there may also be a decrease in the signal, but this would most likely be accompanied by higher voltage peaks due to the movement, and would have a different spectral composition. Thus, it should be possible to distinguish between a decrease in signal strength due to a CSA episode, and a decrease due to the patient moving a further distance from the sensor mat. A technique such as Short Term Fourier Transform could be used to analyse spectral information and allow processing in close to real-time. If the person on the mat had merely moved further away, it would be expected that a breathing signal would still be seen, even though it was weaker than before. It can be observed that the graph in figure 36 above does show a slight ripple during the period of no breathing, and it is not clear why this is the case. It may just be an artefact due to the

filtering and signal processing procedure, or it may be due to interference. Further investigation is needed to discover the source of this ripple effect.

Different types of algorithms will be needed to detect obstructive sleep apnea (OSA), where respiratory effort increases when the airway is blocked, compared with central sleep apnea (CSA), where respiratory effort ceases. For detecting obstructive sleep apnea, we are looking for increased respiratory effort, with a pattern characteristic of a sleep apnea episode starting. For example, the abdominal respiratory effort typically becomes out of phase with the chest respiratory effort during an OSA incident, and this may be detectable by "double peaks" on the breathing movements. Also, the increased magnitude of the breathing movements that occurs during OSA may be detectable, although the magnitude would be expected to vary anyway with patient movements and position. Possibly, the use of multiple detector mats could help improve the detection process, if this was deemed to be viable.

Although it is simple to mimic and test the "central sleep apnea" situation (of no breathing and no respiratory effort) by simple holding of the breath and lying still, it is far less straightforward to test for OSA without data from an actual sleep apnea patient. Ideally, we need to test the device using several volunteers with sleep apnea, and using a pulse oximeter to verify times at which the patient experienced a sleep apnea episode, so that the reliability of the device for sleep apnea detection can be evaluated and improved. Alternatively, the device could be tested with sleep apnea patients during full polysomnography studies, to assess its performance and to obtain useful data to allow optimisation of the signal detection process.

In cases where the patient has a bed partner, there is a risk that the mat will detect breathing signals from the bed partner. One approach to deal with this is for the software to track the breathing of the two people simultaneously. It may be apparent who is who from characteristics of the two signals, or the software may assume that any detected cessation of breathing is always from the sleep apnea patient, and not from the bed partner.

It is desirable to continue further testing, to assess the performance of the detection system with different mattress types and thicknesses, and when the patient is in different positions relative to the mat.

7.2 Generating a "nudge" for sleep apnea interruption

7.2.1 Equipment and methods

A decision was made to use a vibrating motor, similar to those found in mobile phones, to generate a "nudge" to interrupt a sleep apnea episode. This was because mechanical stimulation was thought to be more effective and consistent than audio stimulation, and simpler to implement than electrical simulation or mild electrical shocks, which also had the potential problem of poor skin contact causing poor electrical conductance.

Vibration motors were obtained from Precision Microdrives (www.precisionmicrodrives.com) and the characteristics of selected motors are listed in Appendix A. The 310-101 model of vibrating motor was selected for initial testing, because:

(i) It was self-enclosed with no external moving parts which may catch on clothing, bedding, hair or skin.

(ii) It was compact (10mm diameter) and light.

(iii) It had a fairly high maximum vibrate strength for its size and shape compared with other similar models, with a maximum normalised vibration amplitude of 1.2, and

(iv) It could easily be powered by a 3V lithium battery.

In case the vibrate strength of the 310-101 motor turned out to be too low in practice, a stronger motor was also obtained, and this was a 7mm diameter encapsulated vibration motor with a maximum normalised vibration amplitude of 6. Details are also shown in Appendix A.

The circuit shown in figure 37 below was constructed to control the vibration motor, using a Velleman USB interface board. More information on this USB interface

board is provided in Appendix D. It was necessary to use a driver circuit with a 3V battery, rather than powering the motor directly from the Velleman USB interface board, because the Velleman board is not able to provide sufficient current to actually power the motor. The transistor was selected as being a readily available and inexpensive device that was rated to handle the maximum current, voltage and power that may be needed to drive the vibration motor. The circuit was initially built on a breadboard, and then after successful testing, it was transferred to a piece of copper stripboard.

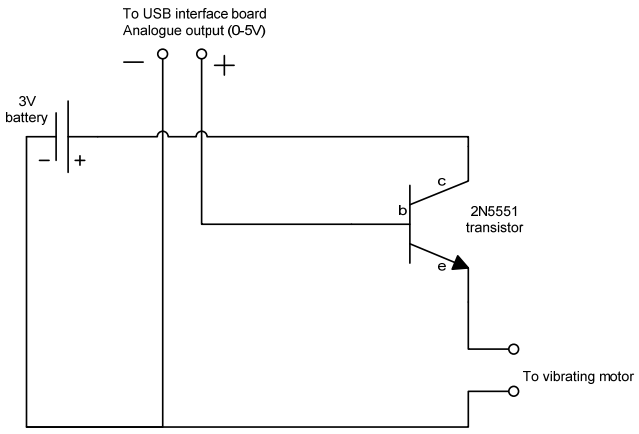


Figure 37: Circuit to control the vibration motor using a computer

Figure 38 below shows a photograph of the Velleman USB interface board, connected to the vibration motor driver circuit. The red wire on the left hand side of the photo are connected to the vibration motor. The USB cable plugs into the connector at the top of the photograph. The battery pack consisted of two 1.5V batteries to give a 3V sources, but a lithium 3V battery could equally well have been used. The battery pack is connected to the copper stripboard.

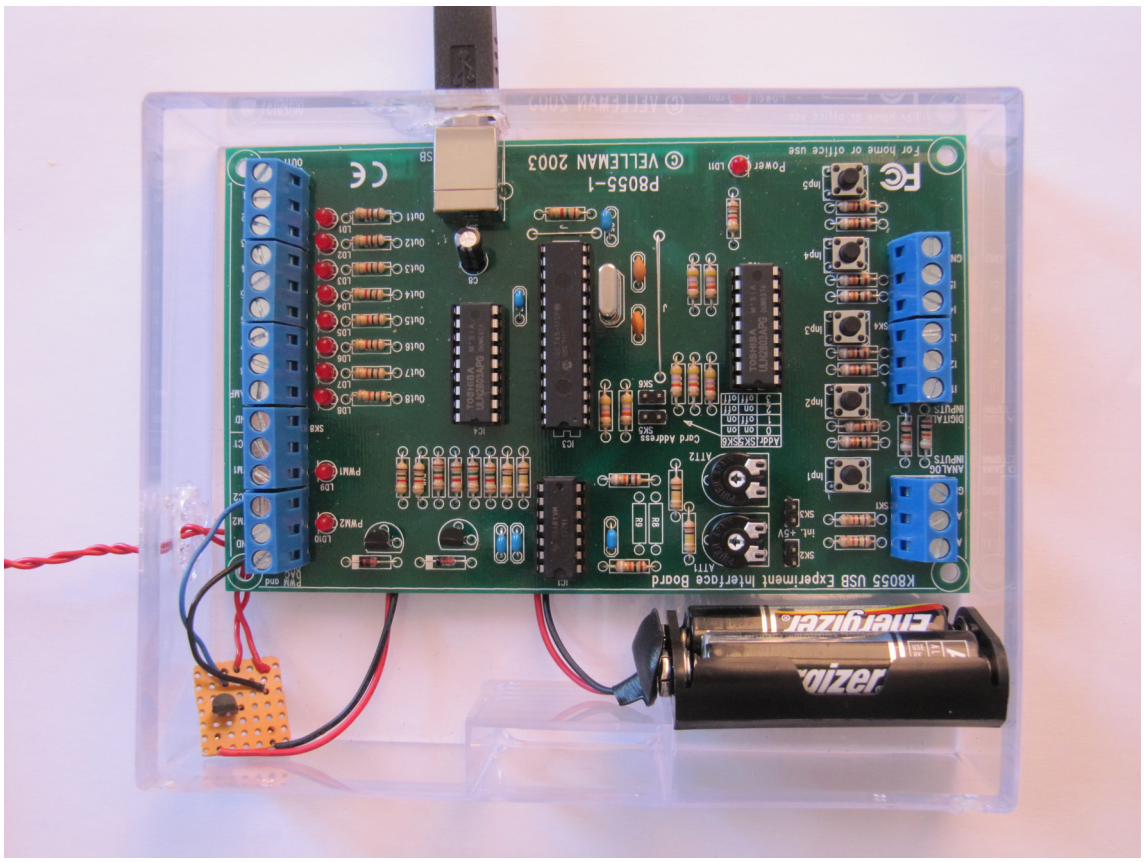
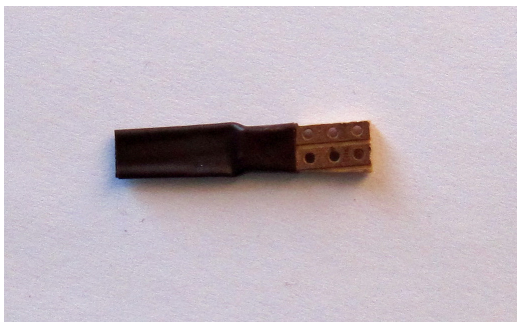


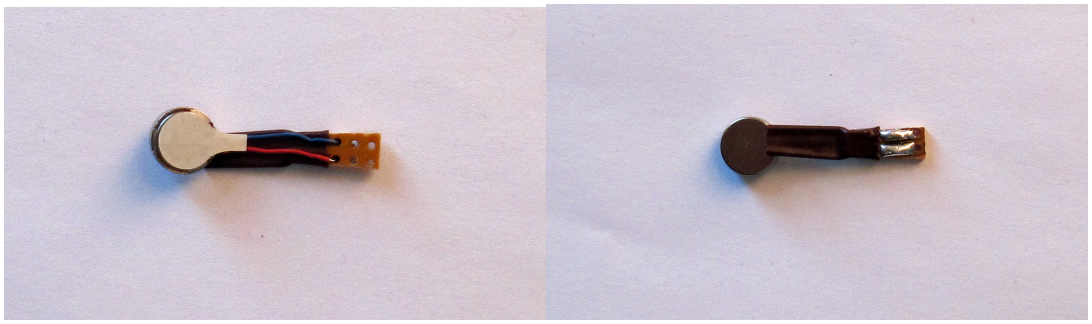
Figure 38: The USB interface board connected to the vibration motor driver

Computer program code, written in the C++ programming language, was used to enable the vibrating device to be activated to different power levels in response to an appropriate analogue output voltage from the Velleman USB interface board. During initial testing, the computer program code was configured to activate the vibrating motor at predetermined times, independent of any measured breathing signals. This was so that an approximate idea of a suitable range of vibration strengths could be gauged. Four different levels of vibration strength were tested out.

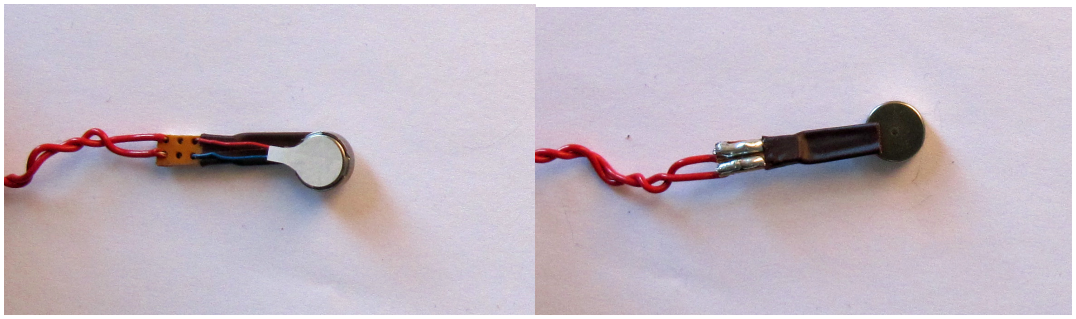
One problem encountered was that the wires on the vibrating motor were very thin, and did not connect well to the thicker wires of the cable, so that the soldered connection was mechanically not robust. To solve this problem, a small piece of copper stripboard was cut, and a small piece of insulating tape wrapped round one end, as shown in the sequence of photographs in figure 39 below.



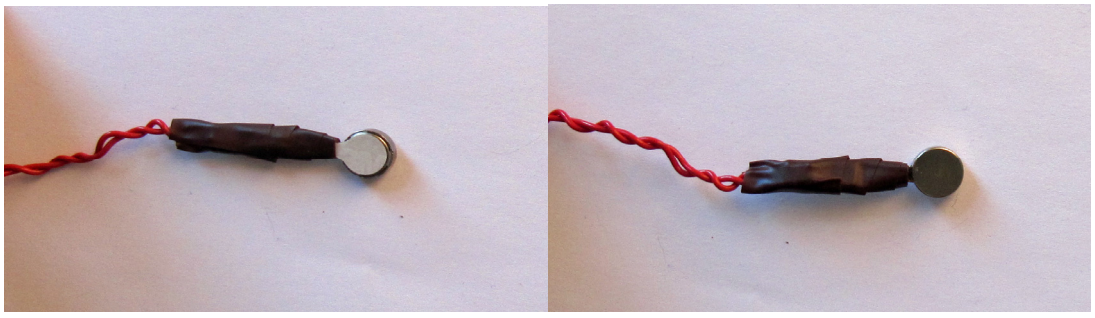
1. A piece of insulating tape was wrapped around one end of a thin piece of copper stripboard.



2. The wires of the motor were soldered to the copper stripboard, so that they lay on top of the tape (top and bottom views shown).



3. The connecting cable was soldered to the other end of the stripboard (top and bottom views shown).



4. The soldered stripboard was then wrapped in insulating tape.

Figure 39: Sequence of photographs showing the mounting of the vibration motor

Originally, the wrist was selected as a location for the vibration motor, and a wrist strap was constructed using Velcro strips and tape, as shown in figure 40 below. However, after trying this out, it became apparent that it could be a problem if the patient moved their arm over a large distance, as there would be a long trailing wire. Thus, instead, the motor was taped under the armpit, using 3M Micropore tape. Other options for positioning the motor on the patient include on the neck, on the stomach area, or under the pillow. The optimum location may turn out to be a matter of personal preference for individual patients.

Figure 40: The use of a Velcro strip as a wrist strap

Another problem encountered was that the motor needs a certain threshold voltage level in order to reliably start. When trying to switch it on at a lower vibrate level, it may start sometimes, but not in a reliable manner. To solve this problem, the software was adapted to apply a short pulse at higher voltage, before dropping the voltage to the desired level.

7.2.2 Results and discussion

Ideally, the testing stages should involve:

(1) The present author testing on herself in order to get an approximate idea of the range of vibrate strengths that may be effective without actually causing an awakening, and

(2) Testing on sleep apnea patients - this has not yet been done, and an ethical approval process must be completed first.

The following testing was done for stage (1) above. A Zeo sleep monitor was used to determine the sleep stage over several hours of the night. The Zeo is described in Appendix E, and comprises a headband with a sensor to determine the sleep stage of the wearer. In a comparison with sleep stages derived in polysomnography, the Zeo appeared to be fairly reliable in performance (Shambroom et al, 2009). The Zeo records sleep stage in 30 second periods, and this data can be transferred to a computer and imported into Matlab to be displayed on a graph.

In addition, the sleep period was recorded on a webcam, to allow any movements or awakenings in response to the activation of the vibrate motor to be recorded and observed. A hand signal to the webcam was used to indicate wakefulness at a time when the vibration motor was activated. The timings from the Zeo, webcam and vibration motor timer were all correlated to within approximately 2 seconds accuracy by using time display on the Zeo sleep monitor, which was clearly visible in the webcam recording. The webcam recording time was calibrated according to the time at which the minute figure changed on the Zeo clock. Figure 41 below shows a still frame from the webcam video. The USB interface board is in a clear plastic box at the head of the bed, and it is controlled by the same computer that is running the webcam. The lower red LED on the interface board indicates that the vibration motor is actively vibrating. This allows the vibration timing to be confirmed and calibrated with the webcam timing. The brightness of this LED indicated the strength of the vibrate pulse. To allow clearer identification of pulse strength, the software code was configured to light up two LEDs for the maximum pulse strength, instead of just a single LED. The upper left red LED on the USB board indicates that the timer is operating on the controller software. The upper right LED is simply a power indicator.

Figure 41: Still frame from the webcam for evaluation of the vibration motor program

Figure 42 below is a graph showing sleep stage during a period of the night, and the red lines indicate times at which the vibrate motor was activated. The letter M indicates a body movement (as recorded by webcam) and the letter W indicates an awakening (as signalled by a hand signal to the webcam). The height of the red lines along the y-axis correlates to the vibration strength.

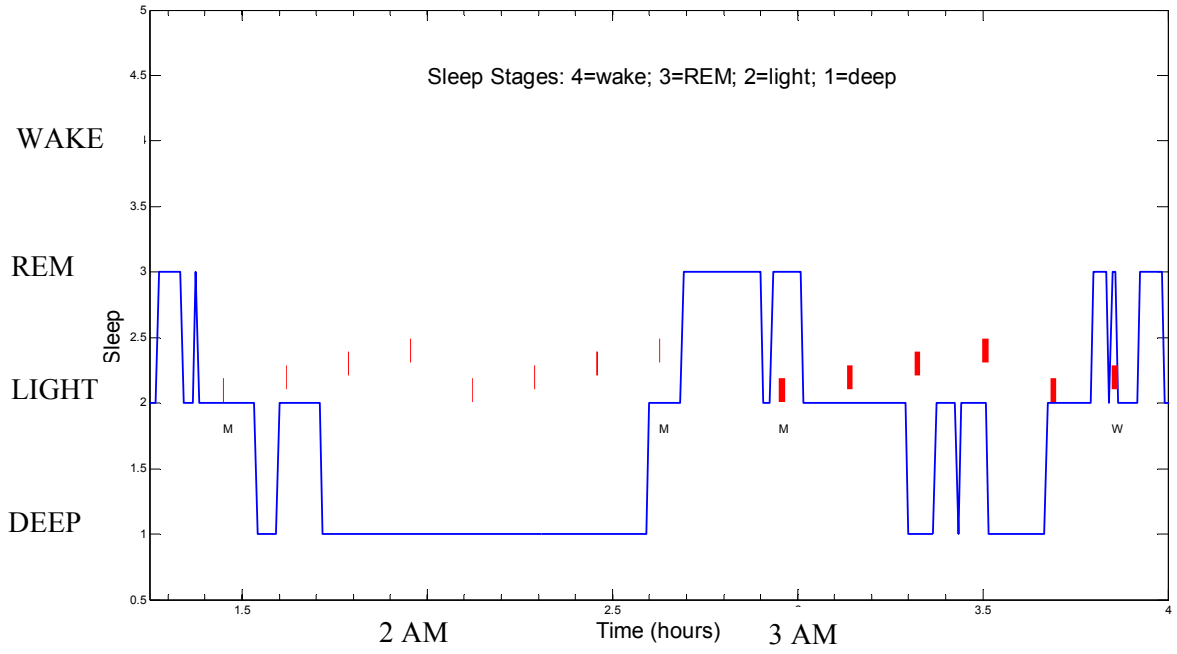


Figure 42: Test hypnogram when using the vibrating motor and timer

It can be observed that two of the body movements occured in light sleep, and one occured during REM sleep. The single awakening occured during REM sleep.

One of the most challenging aspects of the present design is to configure the vibrating device so that it is sufficiently intrusive to induce the patient to move and re-start their breathing, but not so intrusive as to cause the patient to waken up. The above preliminary results appear to suggest that sleep stage is significant in determining the required vibration strength of the motor, as no movements or awakenings were observed during deep sleep. This is a very small data set, and further testing is highly desirable. Test options include using a stronger vibration motor to see if any effect is observed during deep sleep, and using different pulse lengths, pulse ramping functions from low to high, and other variations.

7.3 Use of additional measured signals to improve reliability

To improve the reliability of sleep apnea detection, the signal from the pressure sensitive mat could be interpreted in conjunction with an audio signal of the patient's breathing noises, recorded from a microphone. Ideally, a microphone would also be connected to the computer, to record the patient's breathing noises. The sudden

absence of snoring noises coinciding with an absence of the breathing signal may give a more reliable indication of the onset of a sleep apnea episode. However, it would be desirable to test this on an actual sleep apnea patient.

7.4 A complete sleep apnea detection and interruption system

This section discusses issues involved with connecting the separate components of the system together to form a complete sleep apnea detection and intervention system, using the pressure sensitive mat and the vibrating motor.

In order to create an integrated system, the C++ vibration motor control program may be adapted to also control the USB oscilloscope, and to interact with Matlab for real-time processing and filtering of the measurements. However, another option is to use the Velleman USB interface card for both reading data from the pressure sensitive mat, and for outputting signals to control the vibration motor. This would have the advantage of lowering the cost of the system, and making it available in the form of a single box that requires only a single USB connection. However, the disadvantage of this approach is that the data sampling specification of the Velleman board is rather lower than the data sampling specification of the PicoScope USB oscilloscope. The fact that the maximum sampling frequency of the Velleman board is much lower is unlikely to be a problem, because the frequency of the breathing signal is extremely low (under 1 Hz), and a high sampling rate is not really needed. However, it may be an issue that the Velleman analogue input channels have only 8-bit resolution, and these channels only accept voltages in the range of 0 to 5 volts. The output voltage from the pressure sensitive mat must be appropriately scaled to a 0 to 5V range, to avoid damaging the Velleman hardware, and also to maximise the resolution of the detected signal. If the detected signal is passed to the Velleman hardware in the millivolt range, the limited 8-bit resolution will be effectively much less, and the quality of the recorded data may be insufficient. When scaling the output voltage from the mat, we wish to avoid excessive distortion of the voltage waveform.

Figure 43 below shows a circuit to interface the pressure sensitive mat to the Velleman USB interface board. Diodes are used to limit the voltage and the op-amp is used for amplification of the signal.

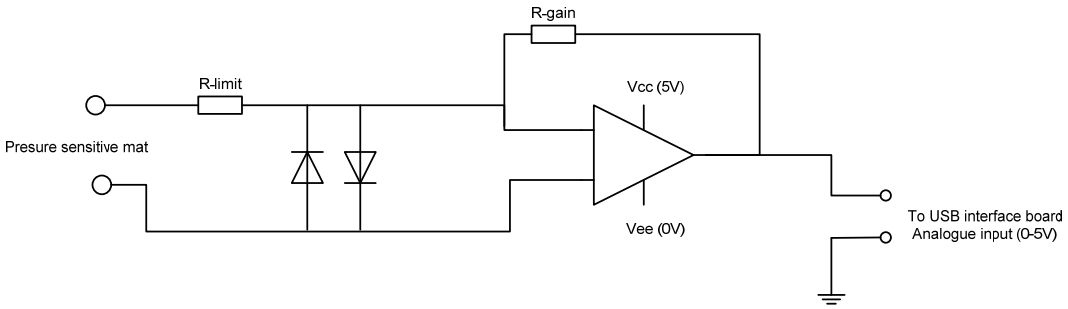


Figure 43: Circuit to connect pressure sensitive mat to the USB interface board

It is still likely there would be issues with the voltage dropping too low to be effectively measured if the person rolled any distance from directly above the mat, because the pressure changes from their breathing would be much weaker. In a more sophisticated option for the circuitry, a non-linear scaling of the signal could be implemented to keep it in the 0 to 5V range, while using as much of that range as possible for best resolution. However, it would then be necessary to take account of this in the subsequent data processing algorithms.

A yet further option is to obtain a higher quality USB board with analogue inputs and outputs, to be used for both obtaining the voltage readings from the pressure sensitive mat and controlling the vibration motor.

The schematic diagram in figure 44 below illustrates a complete system for real-time detection and interruption of sleep apnea episodes. This includes the combined use of an audio detector, as discussed above.

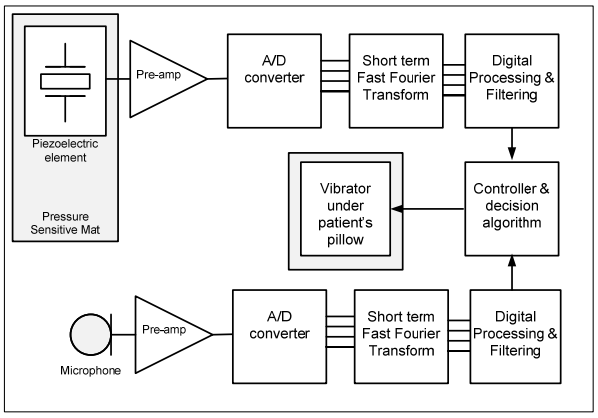


Figure 44: Schematic diagram of a system for sleep apnea detection & vibration treatment

The device may also be utilized as a diagnostic sleep monitor, which can provide overnight recordings of breathing movements. For example, it may provide output data relating to the patient's breathing interval, breathing regularity, and how this varies over an extended period of time.

The existing hardware in the device could be used with suitable algorithms to provide a measurement of additional parameters. For example, it could be possible to make use of the detected heart beat signals from the pressure sensitive mat, instead of just filtering them out, and use them to calculate the heart rate variability (HRV). As discussed in chapter 3, the HRV could be used to monitor for sleep apnea episodes, even though this would not take place in real-time. However, it could be beneficial for providing feedback on how effectively the device was performing, and whether the patient was still experiencing as many sleep apnea episodes. It could even allow the parameters for operating the vibration motor to be adjusted on an automatic basis, using appropriate feedback.

Another option is to attempt to detect the sleep stage using data from the pressure sensitive mat, e.g. as done by Kortalainen (2010) with Emfit sensor foils, and discussed in section 4.2 above. However, to achieve success, it may be necessary to use an array of pressure sensitive mats under the mattress. The advantages of determining sleep stage in this way are that it would avoiding the need for the patient

to wear a band on their head which may fall off, and may be uncomfortable. The disadvantage is that it may give a less reliable classification of the sleep stage.

A further possibility is to extract breathing movement data from the webcam video recording, and correlate this with movement readings from the mat to improve the overall accuracy of detection. When the video is played at fast speed, these breathing movements are very apparent. The disadvantage of this technique for regular monitoring is that it is necessary to keep the light on overnight. The patient could wear an eye mask if the light was a problem for them. Alternatively, the video recording could be performed using an infra-red camera.

7.5 Conclusions

While clearly, there is a lot of development work still needed, the preliminary results for this device do look promising. Even if it is only successful with a subset of patients, it could still provide another treatment option for people who do not achieve great benefit from current treatment options.

8. Overall Conclusions

8.1 Brief summary of findings

It is clear that a pressure sensitive mat with a piezoelectric crystal does have the potential to detect breathing signals in real-time, and with further development work, it could be very useful in sleep apnea detection, particularly with central sleep apnea where no respiratory effort is made. Also, a vibrating motor may have the potential to interrupt sleep apnea episodes for at least some patients, although this may be dependent on their sleep stage. Combining multiple signals may provide a way of increasing the reliability of such a system.

8.2 Further work

8.2.1 Testing the device with sleep apnea patients

Various possibilities for future work have already been discussed in chapter 7 above. The most urgent priority is probably to get some testing done on real sleep apnea patients, and see how well the apparatus performs in this situation. It would be valuable to test on a range of sleep apnea patients, including people with central sleep apnea, obstructive sleep apnea and mixed sleep apnea. Such testing will give an indication of how many false positives are generated, and how many apnea events are successfully resolved, allowing further refinement of the device and the parameters used. It is difficult to obtain this information without testing on actual patients. Ethical approval may be applied for in order to do this testing. Possibly, the testing could be done at Edinburgh Sleep Laboratory, or a similar type of sleep clinic.

8.2.2 Measurement of additional parameters to improve detection

Various options were discussed above. One further option worth mentioning is the use of a throat microphone to pick up breathing and snoring noises. A throat microphone is a type of contact microphone that absorbs vibrations directly from the wearer's throat. It can pick up speech, and even whispers, in extremely noisy environments. If used to detect the patient's breathing noises, it would give a strong signal with low interference.

8.2.3 Wireless vibration motor apparatus

Another development could be to provide a wireless vibration motor stimulator device, by using a miniature wireless receiver to receive a signal from a controller to set the vibrate times and levels. The device would simply consist of a vibration motor, a driver circuit, a lithium battery, and a wireless receiver. This would mean the patient would not have wires trailing out of their bed.

8.2.4 Tattoo sensors

The use of an "electric tattoo" attached to the throat for detecting sounds is described at http://www.bbc.co.uk/news/health-14489208. The tattoo was able to detect differences in words such as up, down, left, right, go and stop. This may have the potential to detect breathing and snoring movements and sounds in a very non-invasive manner. The tattoo is expected to last for up to 2 weeks, before replacement becomes necessary due to the normal process of skin cells flaking off.

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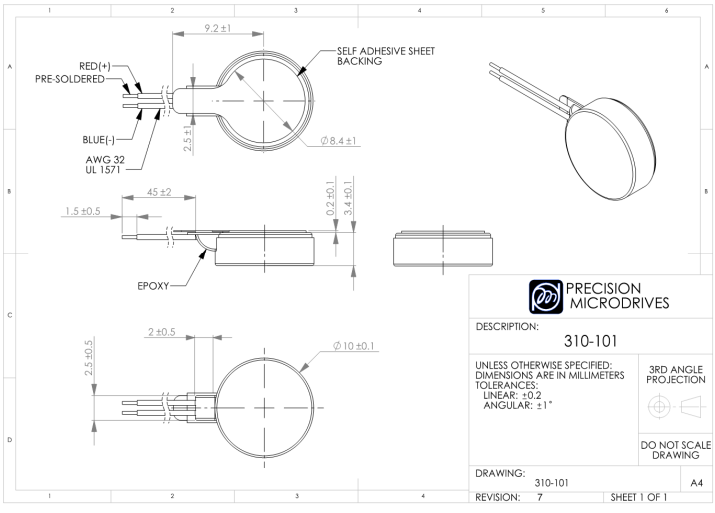
Appendix A: Vibration Motors from Precision Microdrive

The following information was obtained from the Precision Microdrives website, www.precisionmicrodrives.com

10mm Shaftless Vibration Motor (The 310-101 was purchased)

3.4mm Button Type [310-101]

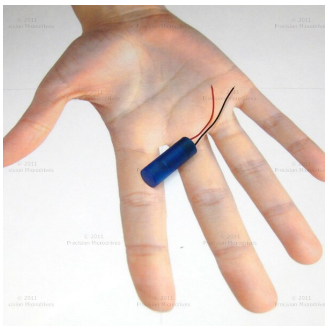
Model	Rated Volts (V)	Physical			Typical		Start		Terminal Resistance (Ohm)	Normalised Vibration Amplitude (G)	Operating Range (V)
		Diameter (mm)	Length (mm)	Weight (g)	Speed (rpm)	Current (mA)	Volts (V)	Current (mA)			
310-101	3	10	3.4	1.2	11200	63	2.1	105	60	1.2	2.1~3.8
310-103	3	10	2.7	1	13500	52	2.3	90	65	0.9	2.3~3.6
310-105	3	10	4	1	14500	59	1.6	95	65	0.95	1.6~3.6
310-109	3	10	2.3	0.8	15000	95	2.3	128		1.2	2.3~3.6
310-113	3	10	3.4	1.2	12000	63	2.3	105	60	1.4	2.3~3.8



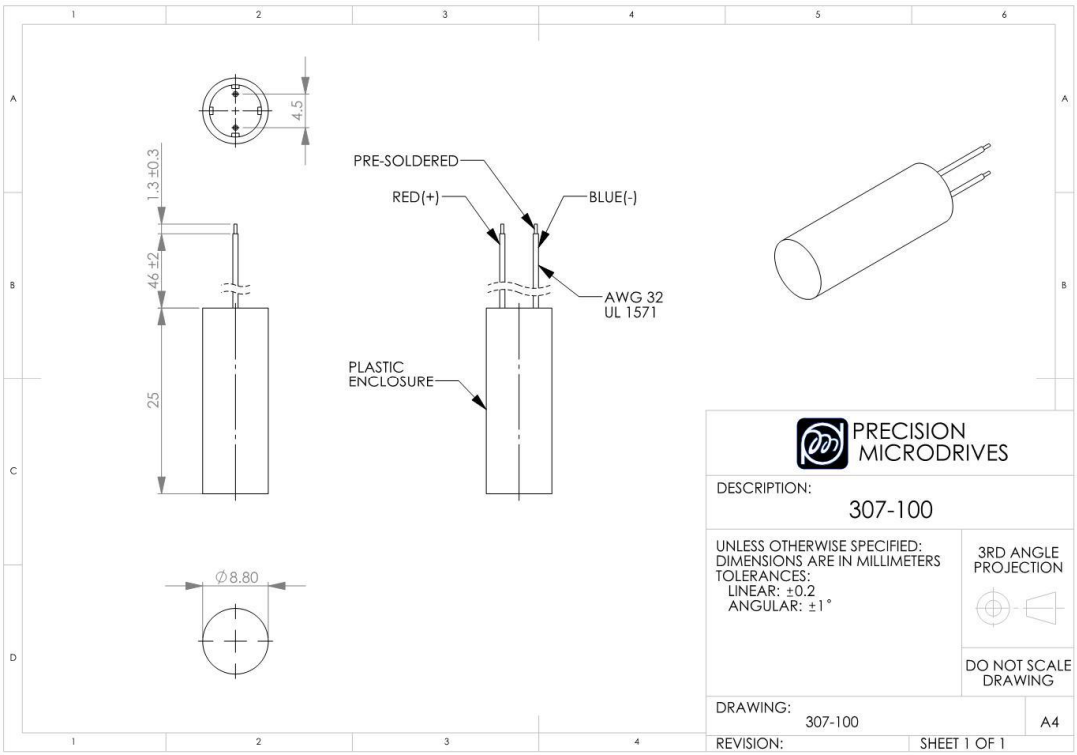
7mm Vibration Motor (Encapsulated)

25mm type [307-100]

Model	Rated Volts (V)	Physical			Typical		Start		Terminal Resistance (Ohm)	Normalised Vibration Amplitude (G)	Operating Range (V)
		Diameter (mm)	Length (mm)	Weight (g)	Speed (rpm)	Current (mA)	Volts (V)	Current (mA)			
307-100	3	8.8	25	4.6	13500	130	0.75	430	5.5	6	0.75~3.6

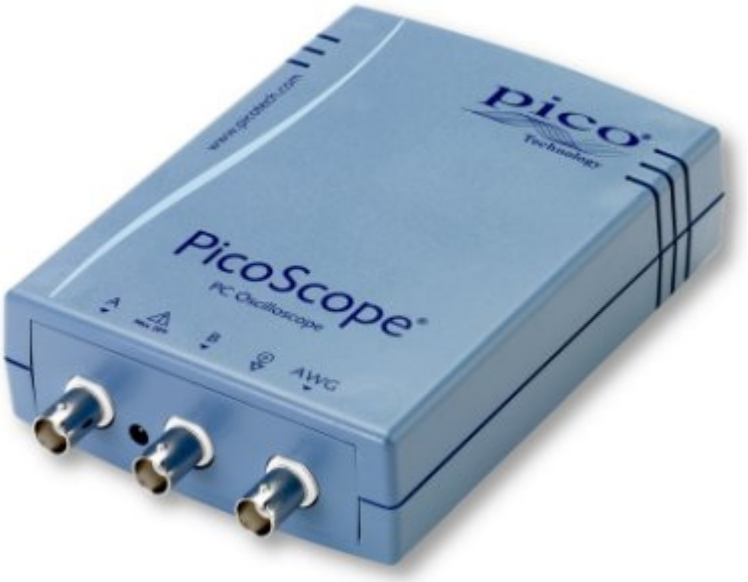


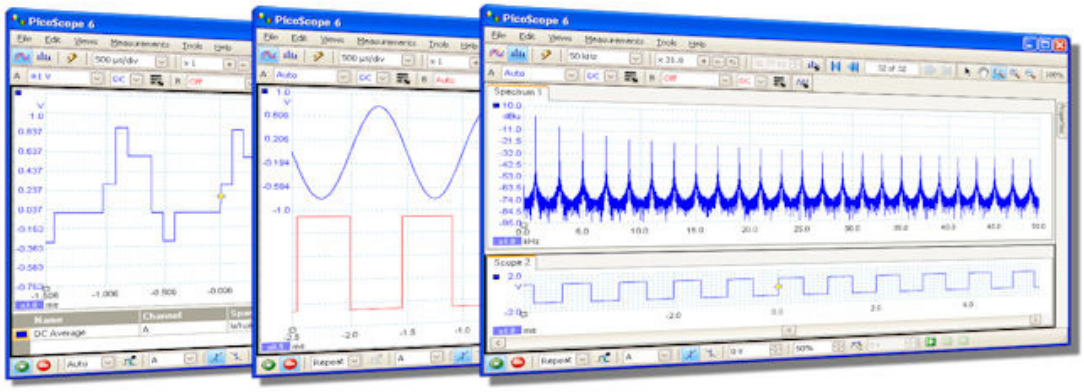
Applications include consumer electronics, hobby and model use, mobile phones, and portable instruments. These motors are designed to be overmoulded by low temperature and pressure plastics and rubbers. These encapsulated motors are water resistant.



Appendix B: Picoscope 2205 USB Oscilloscope

The following information was obtained from the PicoScope website, www.picotech.com





PicoScope 2205 USB Scope Specifications

Oscilloscope - Vertical	
Model	**PicoScope 2205**
Bandwidth	25 MHz
Rise time (calculated)	14 ns

Oscilloscope - Vertical	
Input channels	2
Vertical resolution	8 bits
Enhanced vertical resolution	12 bits
DC accuracy	±3%
Input characteristics	1 MΩ in parallel with 20 pF or less
Input type	Single-ended, BNC connector
Input coupling	Software selectable AC/DC
Input ranges (full scale)	±50 mV to ±20 V in 9 ranges
Overload protection	±100 V (DC+AC peak)

Oscilloscope - Horizontal	
Maximum sampling rate (single shot) **One channel in use** **Two channels in use**	 200 MS/s 100 MS/s
Maximum sampling rate (repetitive signals)	4 GS/s
Maximum sampling rate (continuous streaming mode)	1 MS/s (Record length limited to 2 MS in PicoScope, unlimited when using the supplied SDK)
Buffer memory **One channel in use** **Two channels in use**	 16 kS/channel 8 kS/channel
Buffer memory (in streaming mode)	2 M samples per channel
Waveform buffer	Up to 10000 waveforms
Timebase ranges	50 ns/div to 200 s/div
Timebase accuracy	±100 ppm

Triggers	
Source	Ch A or Ch B
Basic triggers	Rising edge, falling edge, threshold
Advanced triggers	Pulse width, dropout, window, logic

Spectrum Analyser

Spectrum Analyser	
Bandwidth	25 MHz
Frequency range	DC to 25 MHz
Maximum number of bins **One channel in use** **Two channels in use**	 8192 4096
Display modes	Magnitude, peak hold, average
Window types	Blackman, Gaussian, triangular, Hamming, Hann, Blackman-Harris, flat-top, rectangular

Arbitrary Waveform Generator	
Connector type	BNC
Buffer size	4 k words
Vertical resolution	8 bits
Built-in functions	Sine, square, triangle, ramp up and ramp down
Output range	±250 mV to ±2 V pk-pk with ±1 V offset
Output resistance	600 Ω
Clock frequency	2 MHz
Bandwidth	DC to 100 kHz

Physical Properties	
Dimensions	100 x 135 x 45 mm (approx 3.9 x 5.3 x 1.8 in) (Does not include BNC connectors)
Weight	210 g (approx 7.4 oz)

Software	
PicoScope 6 for Windows	**Capture modes**: oscilloscope, spectrum and persistence. **Channel maths**: calculate the sum, difference, product, inverse or create your own custom function using standard arithmetic, exponential and trigonometric functions. **Mask limiting testing**: pass/fail, failure count, total count. **Serial Decoding**: decode data from a serial bus such as I²C. **Automated measurements** **Scope mode**: AC RMS, true RMS, cycle time, DC average, duty cycle, falling rate, fall time, frequency, high pulse width, low pulse width, maximum, minimum, peak–to–peak, rise time and rising rate. **Spectrum mode**: frequency at peak, amplitude at peak, average anplitude at peak, total power, total harmonic distortion (THD %

Software	
	and THD dB), total harmonic distortion plus noise (THD+N), spurious-free dynamic range (SFDR), signal+noise+distortion to signal+noise ratio (SINAD), signal to noise ratio (SNR) and intermodulation distortion (IMD). **Export data formats**: comma separated values (CSV), tab delimited (TXT), windows bitmap (BMP), graphics interchange format (GIF), portable network graphics (PNG), MATLAB 4 format (MAT).
PicoLog for Windows	PicoLog data acquisition software can collect up to 1 million samples. Features include: **Multiple views** - view data as a graph, spreadsheet or text **Parameter scaling** - convert raw data into standard engineering units **Math functions** - use mathematical equations to calculate additional parameters **Alarm limits** - program an alert if a parameter goes out of a specified range **IP networking** - transfer measurements via a LAN or over the Internet
Software development kit	Includes drivers and example code for various programming languages including C, Delphi, Excel, LabVIEW, VEE and Visual Basic.

General	
PC interface	USB 2.0 (USB 1.1 compatible)
Power requirements	Powered from USB port
Compliance	European EMC and LVD standards FCC Rules Part 15 Class A RoHS compliant

Appendix C: BabySense II Pressure Sensitive Mat

The following information was obtained from the Hisense website, www.babysense.net

Babysense II identifies your baby's breathing patterns which are transmitted to a compact microprocessor, in the Babysense II control unit, where they trigger a flashing green light that is clearly visible from a distance. The flashing green light is the signal that all is well, providing a parent or caretaker with peace of mind. If, for whatever reason, the baby's breathing stops for 20 seconds, or slows to less than 10 breathing movements per minute, an audible alarm will sound. On hearing this alarm, a parent or caretaker is alerted to come to the aid of the sleeping baby.

- Simply place two sensors under the crib mattress.
- Sensors monitor entire crib area.
- Sensors do not touch the baby.
- BabySense operates on regular household batteries (no connection to mains).
- Compact, attractive, easy to use design with single switch operation.
- Affordable price – huge benefit.
- If baby stops breathing, BabySense sounds an alarm.
- If breathing slows to less than 10 breaths a minute, BabySense sounds an alarm.
- HiSense is an ISO 9001 / ISO 13485 certified manufacturer.
- BabySense has been extensively tested to ensure your baby's safety and is certified to the requirements of the EC medical device directives.
- BabySense – the first home-use respiratory monitor and the best.

Babysense II infant respiratory movement monitor is highly sensitive and has been proven to be very effective in detecting the cessation of infant breath and sounding an alarm. It does not replace the parent or the caretaker. It is an attention-calling device, and a valuable parent's aid that increases a parent's peace of mind, encouraging a good night's rest. Babysense II cannot intervene when a baby's breathing movements stop. It cannot solve the problem nor can it take action beyond alerting parents and caretakers that the baby needs their assistance. When the Babysense II infant respiratory movement monitor alarm sounds, it is the responsibility of the parent or caretaker to quickly respond to the alarm and take whatever action may be necessary.

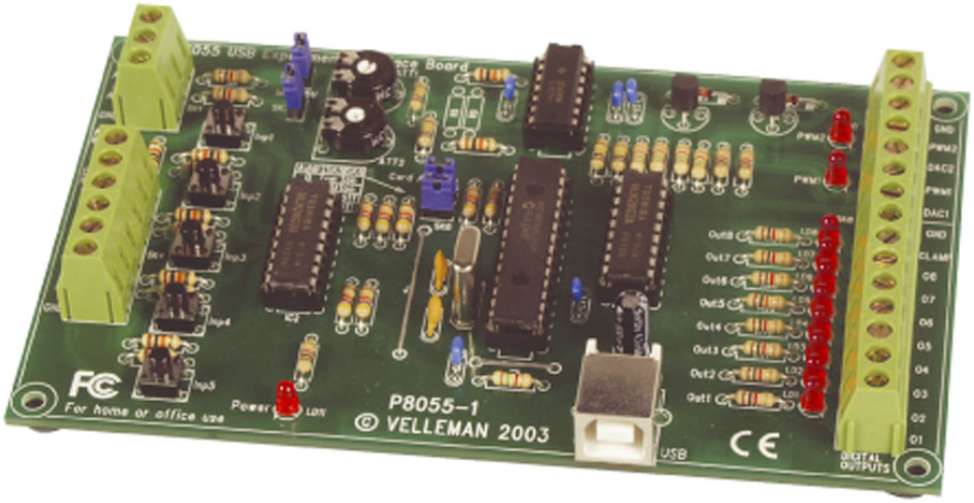
Babysense II is a registered class IIb Medical Device, in accordance with CE Directive 93/42/EEC annex III, VI. (see .pdf links below)
Notwithstanding, premature and high-risk infants must be under supervision of a doctor or health professional.

Hisense, Babysense CU-100_2 Manufacturer Specifications

MODEL Babysense CU-100_2
USE Home
DETECTION TECHNIQUE (APTT INCUBATION) Pressure sensor
AGE GROUP Infant to 3 years
MARKETED SINCE (GRAPHICS DISPLAY) 1992
BREATH DETECTOR
Breath signal (BREATH DETECTOR) Visual
Freq resp, hz (BREATH DETECTOR) 0.3-1.5
Ecg reject circuit (BREATH DETECTOR) Yes
Time delay, sec (BREATH DETECTOR) 20
Sensitivity adjust (BREATH DETECTOR) Automatic
LEAD-FAULT ALERT Visual, audible
Battery used (POWER NEEDED) 4 AA alkaline
Duration,hr 4,000 (6 months)
DIMENSIONS (HXWXD),CM,(IN) 16 x 12 x 3 (6.3 x 4.8 x 1.2)
WEIGHT, kg (lb) (DISPLAY) 0.25 (0.55)
Memory
Other features (MANAGEMENT FUNCTIONS) Analysis of breathing
Documented parameters Respiration waveform
Battery backup Battery operated
Type (CONFIGURATION) Stand-alone
FDA CLEARANCE (Interference compensation) No
CE MARK (MDD) (Interference compensation) Yes
MARKETING REGION (Interference compensation) Worldwide, except North America

Appendix D: Velleman K8055 USB Interface board

The USB interface board was purchased from Maplin Electronics. The following information was obtained from the Maplin website, www.maplin.co.uk and from the Velleman website, www.velleman.be



Specifications:

- 5 digital inputs:(0= ground, 1= open) (on-board test buttons provided)
- 2 analogue inputs:with attenuation and amplification option (internal test +5V provided)
- 8 digital outputs:open collector output switches (max. 50V/100mA) (on-board LED indication)
- 2 analogue outputs:0 to 5V, output resistance 1K5Ω PWM 0 to 100% open collector outputs max 100mA/40V (on board LED indication)
- General conversion time:20ms per command
- Power supply through USB:approx. 70mA
- Dimensions:145(l) x 88(w) x 20(d) mm
- Diagnostic software with DLL included

Appendix E: The Zeo Sleep Monitor

The Zeo Sleep Monitor consists of a wireless sensor mounted on a headband, for detecting sleep stage via ECG measurement, and a base unit for recording the data and for analysis and display. The images below show the base station with docked headband, and the headband on its own. The Zeo can measure and store sleep stage data taken at 30 second intervals throughout the night, and this can be transferred to a computer for detailed review.

Shambroom et al (2009) compares the detection of sleep stages on the Zeo apparatus with polysomnography, as assessed by two separate sleep technicians, and finds a good correlation between the stages indicated on the Zeo (wake, REM, light and deep) with the polysomnography results. Additional information about the performance of the Zeo device is provided at http://www.myzeo.com/pages/52_for_health_professionals.cfm

Appendix F: C Code for Picoscope to Matlab Conversion

The following application was written in C programming code, for converting data files output by the PicoScope data logging software (.csv format) into a format suitable for importing into Matlab (also a .csv format). The code converted any out of range values to a set value, because these were causing the attempted Matlab import to truncate. The code also converted the column format to give just a single column for time and a single column for recorded voltage, deleting the extra column included by the PicoScope data logger.

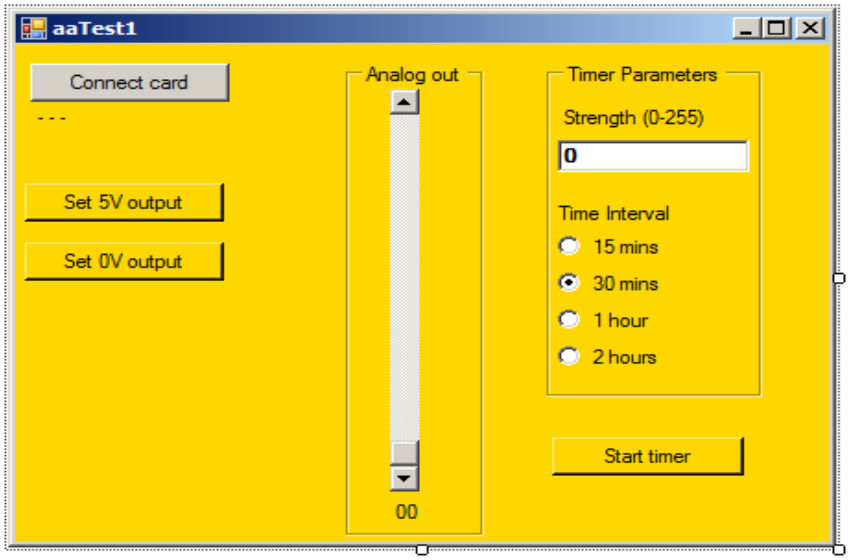
```
/*  C Program to pre-process recorded sleep data from picoscope, for
importing into matlab */

#include <math.h>
#include <stdio.h>
#include <stdlib.h>
#include <string.h>

/* usage: pp <filename stem> */
/* converts fname.csv to fname_pp.csv  */

main(int argc, char *argv[])
{
      #define MAXL 256
      char *filebase, *infile, *dataline;
      char outfile[30], c;
      FILE *finput, *foutput;
      int x, numlines;
      double freq[122], time, voltage;

      char *ptr, *endptr;
      char timestr[25], voltagestr[25];
      int c_one,c_two,oor,i;  /* oor is a count of the number of out
of range values */


      infile = (char *) malloc(30*sizeof(char));
      dataline = (char *) malloc(MAXL*sizeof(char));

    oor = 0;

      /* check that the only command line parameter is the filebase
(i.e. the input filename without extension) */
      filebase=argv[1];
      if (argc!=2)
      {  fprintf(stderr,"\nUsage : pp filebase\nOutput file
filebase_pp.csv\n");
         return(-2);   }

      /* generate input filename from filebase */
      strcpy(infile,filebase); strcat(infile,".csv");

      /* try to open the input file and give an error if this fails
*/
```

```
      if ((finput = fopen(infile, "r")) == NULL)
            {fprintf(stderr, "can't open %s.\n", infile); return(-
1);};

    /* find out the number of lines in the input file */
    numlines = 0;

      while ((c = fgetc(finput)) != EOF)
      {
                  if(c == '\n')
                  {
                        numlines++;
                  }
      }
      fclose(finput);
      printf("Total lines in file: %i\n",numlines);
    finput = fopen(infile, "r");

      /* generate output filename from filebase */
      strcpy(outfile,filebase); strcat(outfile,"_pp.csv");
      printf(outfile);

      /* open output file */
      foutput=fopen(outfile,"w");

      /* read and copy each line of data from input file */
         for(x=0; x<numlines; ++x)
         {   fgets(dataline, MAXL, finput);  /* read the data line
*/

    /* copy the time value from the data line to the output file */
    ptr = strchr(dataline,',');
      c_one = ptr-dataline;       /* c_one = position of first comma
in string */
      for (i=0;i<c_one;++i) (timestr[i] = dataline[i]);
      timestr[c_one]='\0';

           fprintf(foutput,timestr);
           fprintf(foutput,",");

      /* copy the voltage value to the output file */

        //  c_two = ptr-dataline;
      /* c_two = position of second comma in string */
        c_two = c_one+7;

      for (i=0;i<10;++i) (voltagestr[i] = dataline[i+1+c_two]);
      voltagestr[10]='\0';

    if (voltagestr[0]=='*')
      {
            voltagestr[0] = '1';
            voltagestr[1] = '.';
            voltagestr[2] = '0';
            voltagestr[3] = '0';
            voltagestr[4] = '0';
            voltagestr[5] = '0';
            voltagestr[6] = '0';
            voltagestr[7] = '\n';
```

```
            oor++;
        }

            fprintf(foutput,voltagestr);

          }


        /* finish output file with a new line and close input and
output files */
        printf("\nTotal number of out-of-range values in file:
%i\n",oor);

        fprintf(foutput,"\n");
        fclose (foutput);
        fclose(finput);

        return 0;
}
```

Appendix G: C++ Code for Control System

The following windows application was written in C++ code, and designed to make use of the DLL file provided with the Velleman USB interface card:



The following code was used to implement functions for each control:

```
private: System::Void Button1_Click(System::Object^  sender,
System::EventArgs^  e)
                     {
                           int CardAddr = 3;
                           int h = OpenDevice(CardAddr);
                           switch (h)
                           {
                                 case  0:
                                 case  1:
                                 case  2:
                                 case  3:
                                       Label1->Text = "Card " +
h.ToString() + " connected";
                                       Timer1->Enabled = true;
                                 break;
                                 case  -1 :
                                       Label1->Text = "Card " +
CardAddr.ToString() + " not found";
                                 break;
                           }
                     }
private: System::Void Form1_FormClosed(System::Object^  sender,
System::Windows::Forms::FormClosedEventArgs^  e)
               {
                     CloseDevice();
               }
private: System::Void Timer1_Tick(System::Object^  sender,
System::EventArgs^  e)
               {
```

```
                    int buzztime1 = 5;
                    int buzztime2 = 25;
                    Timer1->Enabled = false;
                    int nextbuzz = buzztime1;
                    int buzzlength = 3;
                    seconds = time (NULL) - startt;

              if (seconds < nextbuzz) ClearDigitalChannel(3);
                    if ((seconds > nextbuzz)&&(seconds < (nextbuzz +
buzzlength))) SetDigitalChannel(3);
              if (seconds > (nextbuzz + buzzlength))
ClearDigitalChannel(3);
//                  TextBox2->Text = ReadCounter(2).ToString();

if (count1 != 0)
{
             int hours = seconds/3600;
             int minutes = seconds/60 - hours*60;
             int ss = seconds - minutes*60 - hours*3600;
           Label3->Text = "Time: " + hours + " hours  " + minutes +
" min  " + ss + " sec";
}

                    Timer1->Enabled = true;
             }
private: System::Void Button7_Click(System::Object^  sender,
System::EventArgs^  e)
             {
                  SetAllAnalog();
            VScrollBar2->Value = 0;
                  Label5->Text = (255 - VScrollBar2-
>Value).ToString();
             }
private: System::Void Button6_Click(System::Object^  sender,
System::EventArgs^  e)
             {
                  ClearAllAnalog();
            VScrollBar2->Value = 255;
                Label5->Text = (255 - VScrollBar2-
>Value).ToString();
             }

private: System::Void VScrollBar2_Scroll(System::Object^  sender,
System::Windows::Forms::ScrollEventArgs^  e)
             {
                  OutputAnalogChannel(2, 255 - VScrollBar2->Value);
            Label5->Text = (255 - VScrollBar2->Value).ToString();
             }
private: System::Void Button3_Click(System::Object^  sender,
System::EventArgs^  e)
             {
         if (count1 == 0)
             {
                   startt = time (NULL);
                   Button3->Text = "Stop Timer";
                   Timer1->Enabled = true;
                   Timer1->Interval = 1000;
             Timer1->Start();
             }
```

```
            if (count1 != 0)
                 {
                  startt = time (NULL);
                  Button3->Text = "Start Timer";
                  count1 = -1;
                  Timer1->Enabled = false;
            }
          count1++;

            }
};
}
```

Appendix H: Paper submitted for IEEE PGBiomed 2011

On the following page is a copy of the paper submitted by the present author for the 6th UK and RI Postgraduate Conference in Biomedical Engineering and Medical Physics, held in Glasgow, UK on 14th—16th August 2011.

A NON-INVASIVE SYSTEM FOR REAL-TIME DETECTION AND TREATMENT OF SLEEP APNEA EPISODES

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[2]Scotsig, Glasgow, UK

Abstract - In obstructive sleep apnea, a person's airway becomes repeatedly blocked during sleep, and they waken many times per hour to restore their breathing. Diagnosis is traditionally performed overnight in a sleep laboratory, which is expensive and uncomfortable. Treatment often involves wearing a pressurized mask to keep the airway open. The present authors are developing a new detection/treatment system, using a pressure sensitive mat located under the patient's mattress to monitor breathing movements in real time. Absence of a breathing signal triggers a vibrating device located under the patient's pillow, inducing them to move and resume breathing without awakening.

INTRODUCTION

Sleep apnea is a sleep disorder affecting about 3% of the population. A person's airway becomes blocked during sleep, and they awaken many times per hour to restore their breathing. This can result in excessive tiredness, cardiac problems and other health issues [1]. The standard treatment is continuous positive airway pressure therapy (CPAP), where the patient wears a pressurized mask to keep their airway open. However, this is uncomfortable and is not successful for all patients [2]. Diagnosis of sleep apnea is achieved by polysomnography, which measures multiple parameters overnight in a sleep laboratory, including nasal airflow, body movement, EEG and ECG. An alternative for home monitoring is pulse oximetry [3], but it is not suitable for real-time monitoring, due to a detection time lag of up to several minutes. There is a need for better methods of real-time detection and treatment.

METHODS

Monitoring a baby's breathing with a pressure sensitive mat below the baby's mattress is well-established [4]. A piezoelectric sensor in the mat detects pressure changes resulting from breathing movements. If the movements stop, an alarm is sounded. A key advantage is that it is non-intrusive, making no physical contact with the baby.

The present authors are developing a device for real-time sleep apnea detection and intervention in adults, based on a piezoelectric sensor mat. Digital signal processing is used for improved breathing signal detection. A vibrating device under the patient's pillow is activated if the breathing signal disappears, inducing the patient to start breathing again, preferably without wakening up. Preliminary testing was carried out using a pressure sensitive mat taken from a Babysense™ II baby monitor kit, manufactured by Hisense. The mat was placed under a large, thick cushion (equivalent to a thin mattress), with a person lying on top of it and breathing normally for a period, holding their breath for about 30 seconds, and resuming normal breathing. The voltage from the piezoelectric sensor was recorded to a computer at a 1kHz sampling rate using a Picoscope USB oscilloscope, and imported into MATLAB for processing and filtering.

RESULTS

The measured data was very noisy without filtering, with heartbeats and 50Hz mains hum. Noise was greatly reduced using a 5th order low pass Butterworth digital filter with 0.5Hz cut-off. In figure 1, the filtered signal is superimposed on the measured voltage data. A clear breathing signal is seen at a rate of one cycle about every 5 seconds, leveling off during the breath-holding period and resuming when the breathing re-started.

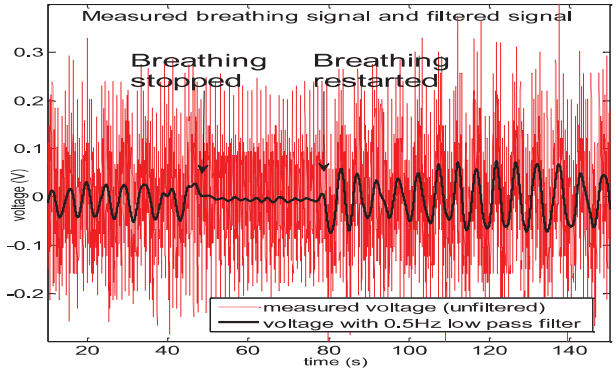

FIGURE 1: Graph of original and filtered pressure measurements from the mat.

A key challenge is to configure the vibrating device to be sufficiently intrusive to induce the patient to move and re-start their breathing, but not so intrusive as to cause the patient to waken up. Initial indications showed vibration strength to be too high, and further work is ongoing.

DISCUSSION & CONCLUSION

The system can pick up breathing signals clearly and easily. Work is ongoing in testing performance with different mattress thicknesses and when a patient is not lying directly above the mat. Further improvements could be made by using more than one mat at different locations under the mattress, and by measuring and combining several different measured variables, e.g. the audio signal of a person's breathing/snoring noises from a microphone, to allow highly reliable detection of sleep apnea episodes.

Further work on the vibrating device to re-start breathing is ongoing. Although intervention by a vibrating device may not be equally successful for all patients, for some patients, this type of system could have the potential to non-invasively reduce the number of nightly awakenings, significantly improving sleep, health and quality of life.

REFERENCES

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[4] J. K. Millns, UK Patent no. GB2192460