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A new system for tailoring and monitoring mechanical ventilation by a wearable device at home

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Pro veritate

adversa diligere…

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Sommario

Le malattie croniche respiratorie sono tra le maggiori cause di morte in tutte le regioni del mondo, esse possono provocare una perdita irreversibile delle funzioni respiratorie a seguito di disfunzioni ventilatorie e di anomalie nello scambio di gassoso o di una combinazione di queste componenti.

La Broncopneumopatia Cronica Ostruttiva (BPCO) è un malattia cronica dei polmoni caratterizzata da un'infiammazione cronica e da una progressiva e irreversibile ostruzione delle vie aeree.

I pazienti affetti da COPD spesso soffrono di alterazioni notturne respiro che risultano nei *Disturbi Respiratori del Sonno* (DRS), caratterizzati da anomalie nel ritmo respiratorio, variazioni nella ventilazione e alterazioni nella struttura del sonno.

Lo scopo di questa tesi è stato di implementare e testare lo ShirtSIG System, un sistema di telemonitoraggio a tempo reale delle condizioni del paziente durante il trattamento con ventilazione meccanica non invasiva nel sonno.

ShirtSIG System è stato realizzato integrando il Chronious Wearable system – un maglietta ergonomica dotata di sensori intelligenti atti a monitorare continuamente i parametri fisiologici del paziente – con lo Home Mechanical Ventilation Monitoring System (HMVMS),un sistema sviluppato dal TBM Lab. Il sistema complessivo permette il monitoraggio costante di diversi parametri di ventilazione e permette al clinico di realizzare una titolazione remota del ventilatore.

Il sistema complessivo stato sviluppato e testato per valutare le sue performance.

I risultati dei test hanno mostrato che ShirtSIG System è in grado di immagazzinare i dati acquisiti in una memoria dedicata e di trasmetterli via Internet. Dato che i dati inviati vengono acquisiti dallo stesso dispositivo, è stato riscontrato che le sue capacità computazionali non sono sufficienti per gestire l'elevato flusso di dati, compromettendo l'affidabilità delle caratteristiche dell'intero sistema. Tuttavia, grazie ai dati trasmessi il clinico può facilmente riconoscere eventi e condizioni patologici specifici ai fini di realizzare una migliore titolazione domiciliare a distanza e di adattarla alle specifiche esigenze del singolo paziente.

Abstract

Chronic respiratory diseases (CRD) are a major cause of adult deaths in all regions of the world and they produce irreversible loss of pulmonary function due to ventilatory dysfunctions, gas exchange abnormalities, or a combination of both.

Chronic Obstructive Pulmonary Disease (COPD) is a chronic lung disease characterised by chronic inflammation and a progressive irreversible obstruction of airflows. COPD patients frequently suffer from nocturnal alterations in ventilation and gas exchange resulting in the Sleep Disordered Breathing (SDB), a group of disorders characterized by abnormalities of respiratory pattern or the quality of ventilation during sleep.

The aim of this work of thesis was focused on the implementation of the ShirtSIG System, a real time telemonitoring system used to monitor the patients' state during non-invasive mechanical ventilation during sleep.

The ShirtSIG System has been realized by the integration of the Chronious wearable system - an ergonomic designed shirt equipped with sensors which allow to monitor continuously patients' physiological parameters - with the Home Mechanical Ventilation Monitoring System (HMVMS) developed by TBM Lab. The whole system allows the constant monitoring of different ventilation parameter and allows the physician to realize a remote titration of the ventilator. The whole system has been developed and tested to evaluate its performances.

The results of the test conducted have shown the ShirtSIG System able to store the acquired data on a dedicated memory and transmit them through the internet. As data coming from two different systems are acquired by the same device, it has been found that its computational capabilities are too low to manage the elevated flow of data, thus compromising the reliability and the real-time features of the whole system.

Nevertheless thanks to the transmitted data, the physician can easily recognize specific pathological events and conditions in order to perform a better titration at patient's home at distance and tailor it on specific needs of each single patient.

Introduzione

La ventilazione meccanica (VM) è una terapia che viene somministrata per assistere o sostituire meccanicamente la ventilazione in soggetti affetti da malattie del sistema respiratorio nei quali è compromessa la capacità di fornire la necessaria ventilazione ai polmoni. La VM viene impiegata spesso su pazienti con patologie croniche respiratorie che richiedono assistenza ventilatoria domiciliare a lungo termine. E' importante garantire un buon adattamento del paziente al ventilatore meccanico nell'ambiente domestico attraverso la titolazione corretta del ventilatore stesso. Attualmente tale procedura viene effettuata in ospedale durante una breve visita che spesso non include un test notturno. Nella prima settimana (dieci giorni) successiva alle dimissioni dall'ospedale, le impostazioni della ventilazione precedentemente fatte potrebbero non essere più quelle ottime per molte ragioni: perché lo stato clinico del paziente potrebbe variare, perché le attività giornaliere del paziente, e quindi il tipo di ventilazione, potrebbero essere differenti da quelle fatte durante la visita di prova e set up dei parametri del ventilatore.

Allo stato attuale dell'arte il personale medico verifica l'adattamento tra paziente e ventilatore tramite delle brevi visite ospedaliere ogni 4-6 mesi, con liste di attesa molto lunghe, e senza la garanzia di una titolazione del ventilatore ottima per il paziente al proprio domicilio. Esistono pochissimi sistemi in grado di permettere al medico un monitoraggio remoto della qualità della ventilazione e un sistema per la titolazione remota offline.

L'obiettivo di questo lavoro di tesi è quello di assemblare e testare un nuovo sistema che permetta al personale medico di poter effettuare il monitoraggio e la titolazione della ventilazione meccanica domiciliare a distanza, in particolare applicata a patologie croniche del sistema respiratorio, al fine di ottimizzare la terapia ventilatoria fornita.

Il primo capitolo fornisce una breve introduzione all'anatomia del sistema respiratorio e alle malattie che lo possono colpire, in relazione allo scopo di questo lavoro: la malattia cronica ostruttiva polmonare (COPD), disturbi sonno correlati (SDB) e la sindrome dell'apnea notturna (SAS).

Il secondo capitolo contiene una panoramica sull'attuale stato dell'arte delle tecniche di

telemonitoraggio remoto di pazienti cronici domiciliati, evidenziandone i limiti dovuti principalmente alla mancanza di interazione in tempo reale tra medico e ventilatore in funzione e alla impossibilità da parte del personale ospedaliero ad intervenire per modificare le impostazioni del ventilatore a seconda delle necessità del paziente.

Un aspetto importante descritto in questo capitolo è una panoramica su due sistemi implementati in progetti precedenti. Un dispositivo descritto permette la connessione remota in tempo reale tra paziente (ventilatore meccanico) e medico, il quale può visualizzare in tempo reale i parametri di respiro del paziente (pressione, flusso, perdite, volume corrente) dall'ospedale grazie ad una connessione ad internet e può intervenire cambiando i parametri di ventilazione del dispositivo domiciliare. Il secondo dispositivo introdotto è parte di un progetto europeo (Chronious) ed è composto da un sistema indossabile per il monitoraggio remoto offline di vari parametri fisiologici (movimenti di addome e torace, pulsossimetria, ECG, temperatura, umidità…). L'utilizzo dei due sistemi integrati permette il monitoraggio remoto in tempo reale della ventilazione meccanica somministrata attraverso un più completo set di parametri che aiuta il personale medico a titolare e monitorare la terapia ventilatoria somministrata in modo più accurato ed adatto alle condizioni del singolo paziente.

Il capitolo terzo è dedicato alla descrizione del dispositivo nella sua integrità, sia dal punto di vista hardware che software. Viene inoltre descritto il lavoro che è stato effettuato per unificare i due sistemi differenti in un articolato e più completo dispositivo in grado di campionare segnali provenienti sia dal ventilatore meccanico domiciliare che dal sistema indossabile, entrambi utilizzati durante il sonno dei pazienti.

Il primo sistema è composto da un dispositivo basato su un microprocessore su cui è installato linux embedded e che viene connesso tramite protocollo USB al ventilatore meccanico e ne campiona i segnali di pressione, flusso, perdite e volume corrente. Tali segnali vengono salvati in una memoria interna insieme ai parametri campionati dal sistema indossabile il quale tramite una connessione Bluetooth li comunica al sistema principale. Il sistema indossabile è composto da una maglietta fatta di materiale elastico in cui sono cucite due bande elastiche per la misura degli spostamenti toracici ed addominali, quattro elettrodi per l'elettrocardiografia, un pulsossimetro a riflettenza, un sensore ambientale per misurare temperatura ed umidità ed un accelerometro per determinare la posizione del paziente.

Il sistema principale si connette ad internet tramite un modem GPRS ed agisce da server attendendo la connessione da parte del computer remoto del personale medico, il quale, una volta autenticato, tramite apposito software è in grado di visualizzare le tracce di tutti i parametri in tempo reale e di modificare le impostazioni del ventilatore da remoto.

Il quarto capitolo descrive i test, effettuati su soggetti sani, a cui è stato sottoposto il sistema realizzato per verificarne funzionalità e affidabilità. Anzitutto è stata testata la capacità del sistema finale di acquisire i dati in tempo reale da entrambi i sistemi senza perdita di informazione o compromissione della caratteristica di tempo reale. Il sistema ha mostrato delle fragilità da questo punto di vista dovute in gran parte alla scarsità della capacità di calcolo del sistema centrale, non sufficiente per gestire il campionamento da due sistemi complessi.

I test successivi sono stati effettuati utilizzando una versione alleggerita del sistema in modo da poter verificare il funzionamento su lungo periodo, ovvero durante l'acquisizione notturna di 8 ore. Inoltre è stata testata e dimostrata l'affidabilità del sistema in termini di segnali visualizzati sul terminale del personale medico, sul quale è possibile riconoscere e discriminare gli eventi tipici delle patologie in esame, quali ad esempio apnea ostruttiva o centrale e respiro paradosso.

Il capitolo quinto riporta le conclusioni riguardo il sistema complessivo, evidenziando la necessità di potenziare la tecnologia utilizzata per mantenere la condizione di tempo reale senza perdita di informazione e evidenzia la necessità di verifica del sistema su pazienti COPD e SAS.

Il sistema ha dimostrato possibilità di adattamento e scalabilità e la sua utilità per la titolazione ed il monitoraggio remoto di pazienti respiratori cronici al loro domicilio.

Chapter 1 - Anatomy, physiology and pathologies of the respiratory system

1.1 Introduction

Respiration is the motor of life; it is one of the seven characteristic processes shared by all living organisms together with movement, sensitivity, nutrition, growth, excretion ad reproduction.

Breathing in an essential function and must occur all the day time during the life, in the conscious or unconscious state, awake or asleep.

The main respiratory function is to attempt gas exchange with the environment, delivering oxygen to the body metabolism, and removing carbon dioxide and other residual substances consequentially produced, which are toxic for the cells and must be expelled from intracellular environment.

The respiratory and circulatory systems act together to achieve these functions.

With their action, respiration and circulation, contribute to correct conditions for metabolism, providing the requested amount of oxygen to the tissues and removing carbon dioxide from the body. (Figure 1.1).

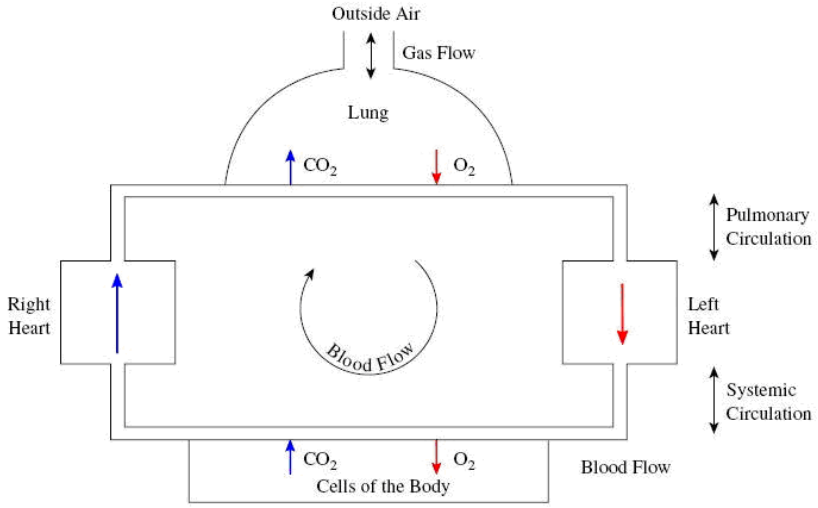


Figure 1.1 - Schematic overview of the respiratory and circulatory systems action totransport oxygen from the outside air to the peripheral cells and to transport carbon dioxideback from the cells to the outside air.

The respiratory system not only achieve to gas exchange but provide a defence against bacterial, viral and other infectious agents, regulates temperature, and stabilizes blood acid-alkaline balance (pH), playing a fundamental role in the whole body homeostasis.
The impairment of one or most of this function leads to a pathological state that affects normal breathing. This can cause alterations in respiratory system structure and function, finally leading to a condition of *respiratory disease*.
Respiratory diseases can arise from a number of causes, including inhalation of toxic agents, accidents, and harmful lifestyles, such as smoking, infections and genetic factors, either directly or indirectly, and can affect one or more parts of the respiratory system.
Some of them may temporary and relatively harmless; others may be life-threatening and persists during the all life time: these lasts it can be classified as *chronic respiratory disease***.**
Chronic respiratory diseases (CRD) are the major cause of premature adult deaths in all regions of the world in the developed as well as in the developing countries [57].
Impairments caused by chronic diseases of the respiratory system generally produce irreversible loss of pulmonary function due to ventilation dysfunctions, gas exchange abnormalities, or a combination of both.
One of the most widespread and cost-effective [49] CRD is Chronic Obstructive Pulmonary Disease (COPD).
Chronic obstructive pulmonary disease (COPD) is a chronic lung disease characterised by a progressive obstruction of airflow that cannot be fully reversed. It is considered the fourth leading cause of death, affecting 14 millions adults in the United States [57], and the previsions sets it to be the third by 2030.
Active smoking remains the main risk factor, but other factors are becoming better known, such as occupational factors, infections and the role of air pollution [59].
COPD is often associated with significant comorbidities.
For example patients with COPD frequently suffer from nocturnal alterations in ventilation and gas exchange resulting in *sleep disorders breathing.*
Sleep-Disordered breathing (SDB) describes a group of disorders characterized by abnormalities of respiratory pattern or the quantity of ventilation during sleep [19].
The consequences of the abnormal breathing during sleep include excessive daytime sleepiness, hypertension, stroke risk, myocardial infarction, heart failure, metabolic

dysfunction and neurocognitive dysfunction [15, 16, 17]: sleep-disordered breathing indeed, adversely affects daytime alertness and cognition and is associated with cardiovascular disease, particularly in men aged 40–70 years[25]. There can be recognized several types of breathing disorders during sleep; symptoms may include snoring, pauses in breathing, and disturbed sleep.

Most widespread of them are sleep apneoa-hypopneoa syndromes, that are central and obstructive apnoea syndromes.

Sleep-disordered breathing (mainly obstructive sleep apnoea OSA) and COPD are among the most common pulmonary diseases, so a great number of patients have both disorders; substantial number of patients will have both OSA and COPD.

This common combination of OSA and COPD has important implications for diagnosis, treatment, and outcome. Specifically, patients with COPD and OSA have a substantially greater risk of morbidity and mortality, compared to those with either COPD or OSA alone [75, 76, 77].

The goals of therapy for subjects affected by such combination is to improve lung mechanics as well as gas exchange ultimately leading to better sleep quality and health status: currently, treatment consists on the application of nocturnal non-invasive mechanical ventilation to the patients.

In the first part of this chapter, the general anatomy and physiology of the respiratory system will be analysed.

The second part, instead, offers a description of the of COPD and sleep apnoeas in order to better understand the pathophysiological mechanisms that can make nocturnal continuous monitoring a useful aid to titration during NIPPV treatments.

1.2 Anatomy of the human respiratory system

In mammals the *respiratory system* consists of the set of organs and tissues that contribute to capture oxygen from the environment and give out the carbon dioxide that is produced as a result of metabolism within the cells [1].

The main components of the *human respiratory* system are *lungs* where gas exchange between blood and air take place, the *airways* that connect the lungs to the outside environment, and the structures in the chest - *rib cage and diaphragm* - involved with the respiration movements that bring air in and out of the lungs. (Figure 1.2).

The airways are divided in the *upper airways*; include the nasal passage, the oral cavity the pharynx and larynx, and the *lower airways* comprise, the trachea, bronchi.

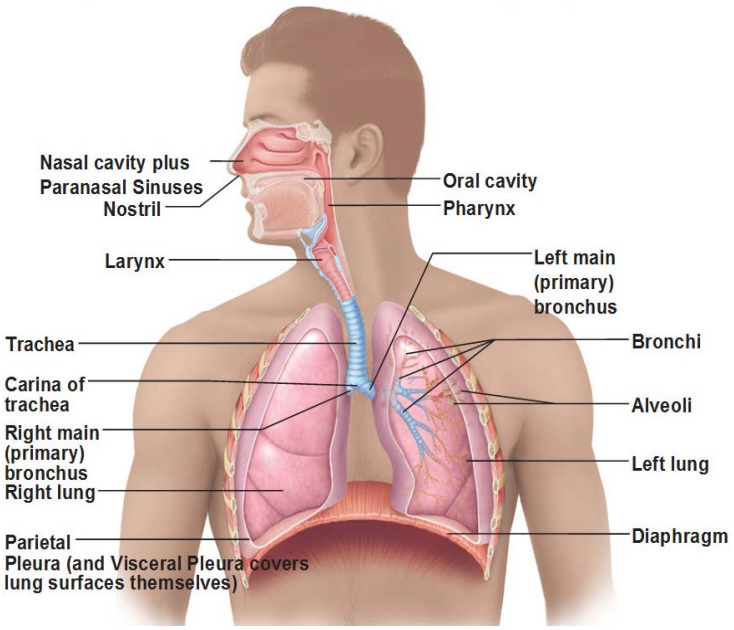


Figure 1.2 - Anatomical Overview of the respiratory System

1.2.1 Upper Airways: nose, mouth, pharynx and larynx

Breathing starts at the nose and the mouth.

The upper airways, is in the fact, the primary conduit for passage of air into the lungs. Air enters the body through the nose, and is gradually warmed, humidified and partially filtered: these functions together realized the primary air condition by the upper respiratory airway.

The filtration function of upper airways [3] is made in two principal ways:

- *By the hairs and cilia* at the entrance to the nostrils, important for filtering out large particles.
- *By turbulent precipitation;* the air passing through the nasal passageways hits many obstructing vanes and the particles suspended in, having far more mass and momentum than air, cannot change their direction of rapidly as the air can. Therefore, they stop and remain entrapped in the mucous coating.

The filtration function is reduced in mouth breathing. For example, if nasal respiration removes SO2 25 ppm concentrated, this capacity is reduced of 65% in oral ventilation [6].

After the nose and the mouth, the airflow continues into nasal passages through pharynx, a fibrous-muscular channel, common to both the respiratory and the digestive system, where filtering and warming processes go on. The larynx is a tube-shaped organ in the neck that contains the vocal cords. The larynx is about 5 cm long. It is part of the respiratory system and is located between the pharynx and the trachea [5].

Ordinarily, the temperature of the inspired air rises to within 1°F of body temperature and to within 2 to 3 per cent of full saturation with water vapour before it reaches the trachea[3].

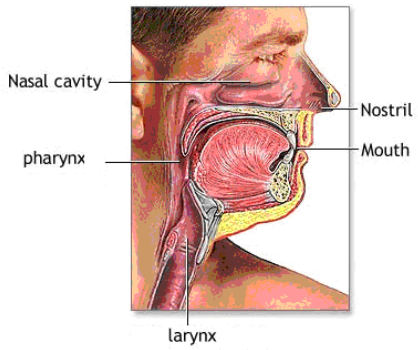


Figure 1.3 - Upper Airways

Structurally, the upper airways are a collapsible, compliant tube; both passive mechanical

and active to neural influences contribute to its patency and collapsibility.

This total structure forms a passage for movement of air from the nose to the lungs and also participates in other physiological functions such as phonation and deglutition.

The properties of the upper airways are a compromise between these different functions, which variably require maintenance of patency, during breathing, or closure of the airway, as in swallowing [7].

Modification of the structural properties of the upper airway may lead to respiratory dysfunction that can affect the whole respiratory system.

1.2.2 Lower Airway: trachea, bronchi, alveoli

The lower respiratory tract, or *lower airways*, extends from the larynx to the most distal portions of the lung parenchyma airways and consists of a series of branching tubes which become narrower, shorter, and more numerous as they penetrate deeper in to the lung [5].

Starting from the trachea, which divides in to right and left main bronchi the process, continues down to the terminal bronchioles: it can be distinguished 23 generations of bronchi in the trachebronchial tree (Figure 1.4).

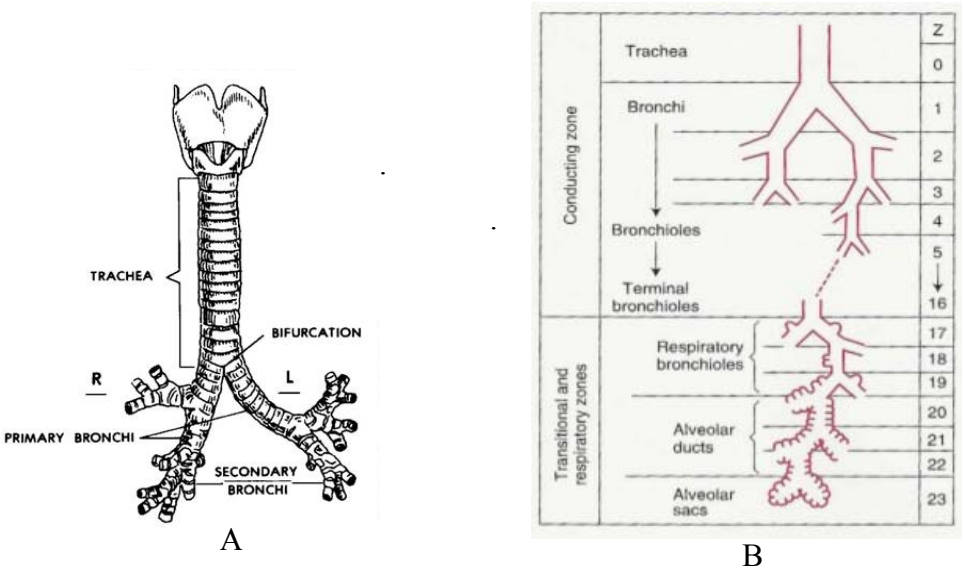


Figure 1.4 – LowerAirways:

A.Tracheobronchial Tree B.Division of lower airway in smaller-diameter ducts

Proceeding down toward the lungs, the diameter of the single duct became smaller, but the number of ducts increases. Total section gradually reduces and the consequential fluidodynamics makes the air flow speed decreased near to zero into the alveoli.
Functionally lower airways can be considered in two groups: conducting and transitional. The former comprises those whose walls do not contain alveoli and are thick enough to prevent gas diffusing into the adjacent lung parenchyma. They include the first sixteen generations of bronchi, the trachea, bronchi, and membranous non-alveolated bronchioles. Their main functions are humidification, purification and gas transportation.
Because the conducting airways contain no alveoli and therefore take no part in gas exchange, they constitute *the anatomic dead space*: its volume is about 150 ml [5].
The *transitional airways*, instead are starting from the seventeenth generation of bronchi: these are named *respiratory bronchioles [6]*, structurally defined by the absence of cartilage in their walls because the function of transportation is gradually replaced by the function of diffusion.
These airways, along with their accompanying arteries and veins, lymphatic vessels, nerves, interlobular septa, and pleura, constitute the non-parenchymal portion of the lung.
As the name suggests, transitional airways have both conductive and respiratory functions: in addition to conducting gas to and from the most peripheral portion of the lung, each has alveoli on its wall that serve in gas exchange.

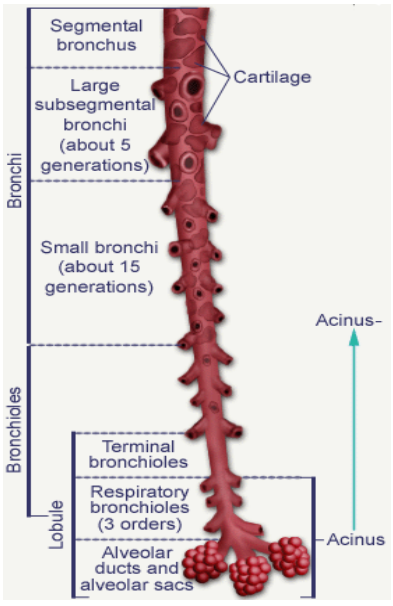


Figure 1.5 - Respiratory Bronchioles and terminal airways

Alveoli associated with the transitional airways and with the more distal alveolar sacs constitute the *lung parenchyma*. It has been estimated that approximately 87% of the total lung volume is alveolar, 6% of which is composed of tissue, and the remainder of which is gas. [1].

There are almost 130.000 respiratory bronchioles connected to the same number of acini - that is a cluster of ducts and alveolar sacs – each of them, about 3.5 mm large.

Respiratory bronchioles divide into alveolar ducts (generation 20-22), and alveolar sacs on which walls develops almost the 50 percent of the alveoli (Figure 1.5).

1.2.3 The lungs

All the structure previously described concurred in the composition of the lungs.

The lungs are a pair of spongy, air filled organs located on either side of the chest: their primary function is the gas exchange between air and blood. (Figure 1.6).

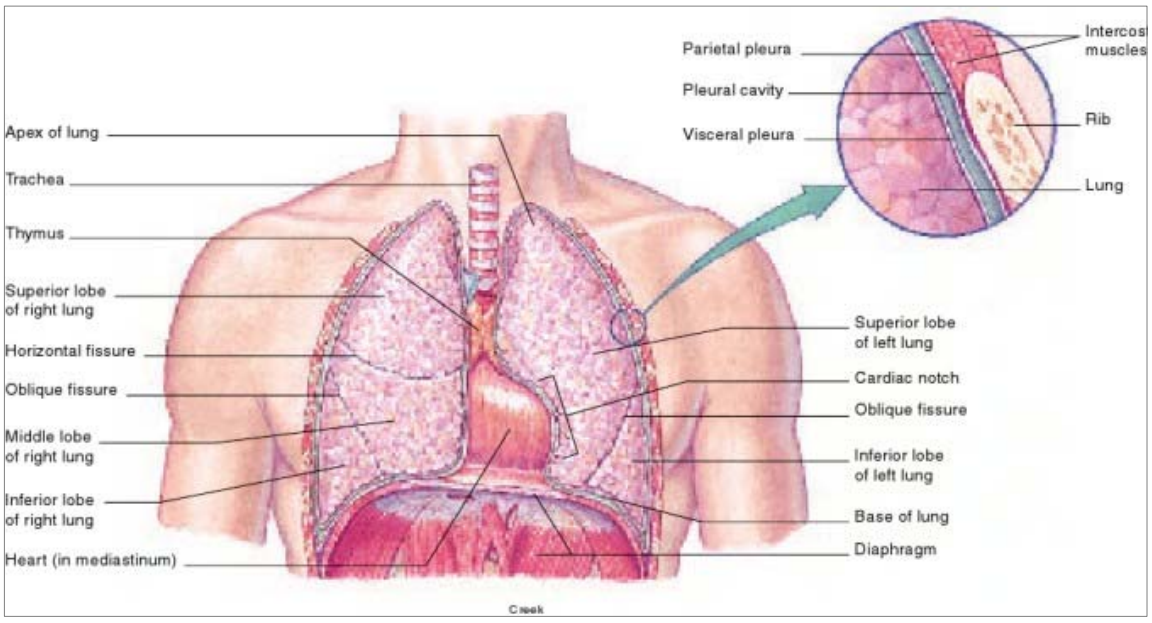


Figure 1.6 - The lungs

The lungs are protected by the ribcage and are covered, as the inside of the whole chest cavity, by a two-layer elastic tissue layer called the *pleura*.

A thin layer of fluid in the *pleural cavity* acts as a lubricant allowing the lungs to slip smoothly as they expand and contract with each breath.

The space between both lungs is occupied by the heart, the two main bronchi that transport gas to and from both lungs, and the oesophagus which leads to the stomach [4].

The *diaphragm* stays at the bottom of the lungs there and is a thin dome-shaped skeletal muscle that extends across the bottom of the rib cage.

The diaphragm plays an important role in breathing: it contracts with each inspiration, enlarging the volume of the thoracic cavity This reduces intra-thoracic pressure, which creates a depression that draws air into the lung. [6].

The right lung is larger in volume and shorter than the left lung. The left lung must leave room for the heart. The right lung is divided into three pulmonary lobes (*upper, middle and lower*) and 10 bronchopulmonary segments .

The left lung is smaller and narrower than the right lung and is divided into two pulmonary lobes (upper and lower) and eight bronchopulmonary segments.

A pulmonary lobe is a major subdivision of a lung marked by fissures: each lobe is further partitioned into bronchopulmonary segments, composed by many small compartments called lobules (Fig.1.7)

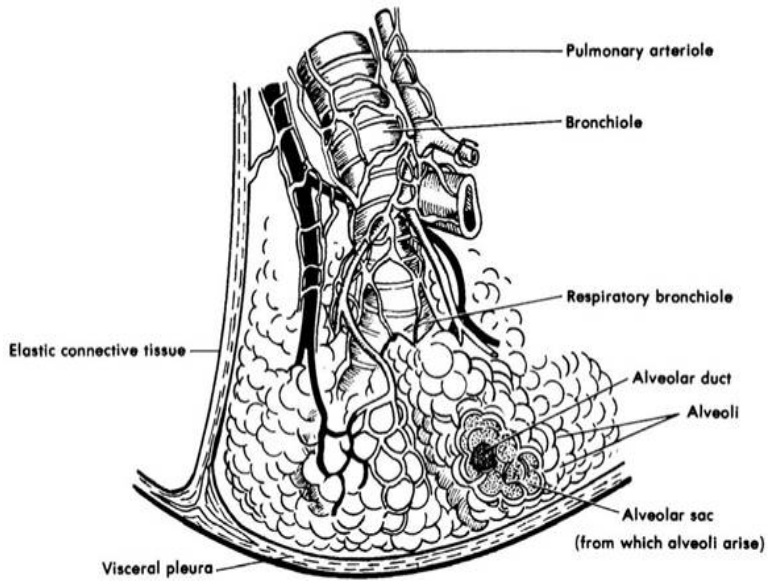


Figure 1.7 - Lung lobule

There are about 300 million alveoli in the human lung, each about 0, 3 mm in diameter.

Their total surface would be 85 square meters, but their volume only 4 litres. By contrast, a single sphere of this volume would have an internal surface area of only 1/100 square meter.

Thus, the lung gene rates this large diffusion area by being divided into myriad units.

1.3 Physiology of respiration

1.3.1 The act of breathing

In order to breathe, we must continuously contract and relax our respiratory muscles about 30,000 times a day, and billion times for a lifetime [1].

The respiratory muscles (Fig 1.8) move the parts of the chest wall that form the boundaries of the thoracic cavity, either enlarging or contracting their volume and thereby ventilating the lungs.

They act as a *ventilatory pump.*

This ventilatory pump is obviously essential for life and its action is to replenish the alveoli with fresh air (*inspiration*) and to expel alveolar gas from the lung (*expiration*).

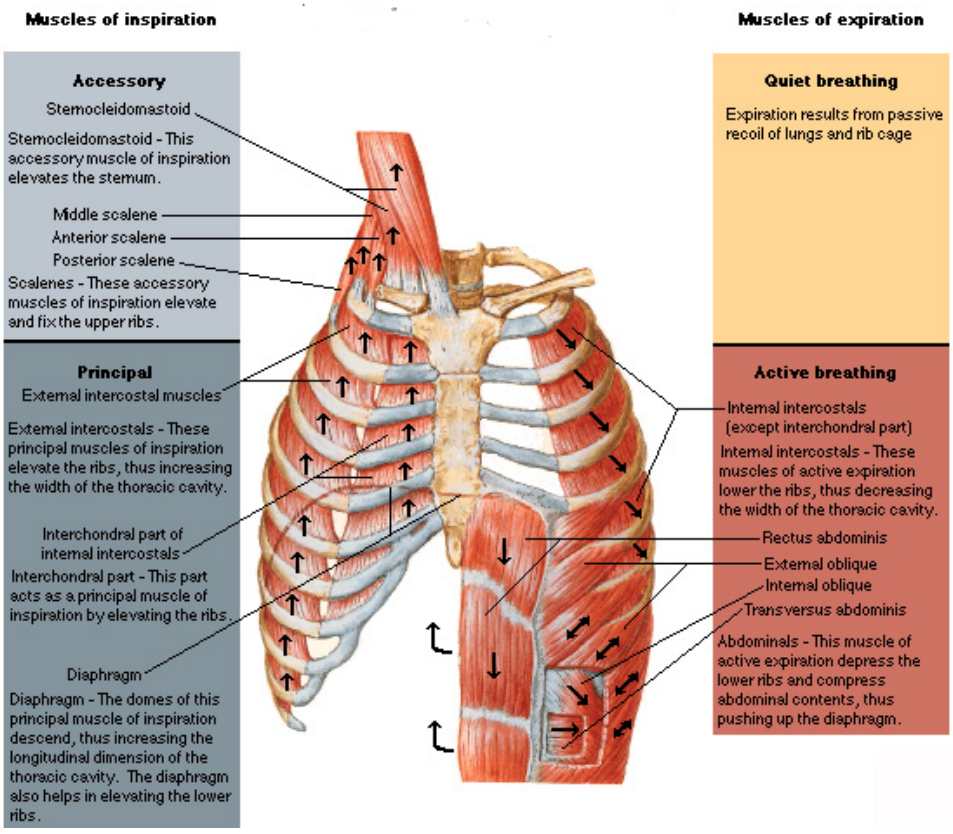


Figure 1.8 - Muscles of Breathing. All the muscles that elevate the chest cage are classified as 'muscles of inspiration', those muscles that depress the chest cage are classified as 'muscles of expiration'.

The lungs can be expanded and contracted in two ways:

- by downward and upward movement of the diaphragm to lengthen or shorten the chest cavity,
- by elevation and depression of the ribs to increase and decrease the anteroposterior diameter of the chest cavity.

In normal quiet breathing the first method almost entirely persists, by the movement of the diaphragm.

During inspiration, contraction of the diaphragm pulls the lower surfaces of the lungs downward. Then, during expiration, the diaphragm simply relaxes, and the elastic recoil of the lungs, chest wall, and abdominal structures compresses the lungs and expels the air.

In heavy or *active* breathing, instead the second method occurs because lungs need to expand more, and the action of diaphragm and the elastic forces are not powerful enough to cause the necessary rapid expiration, so that extra force is achieved mainly by contraction of the *abdominal muscles*, which pushes the abdominal contents upward against the bottom of the diaphragm, thereby compressing the lungs.

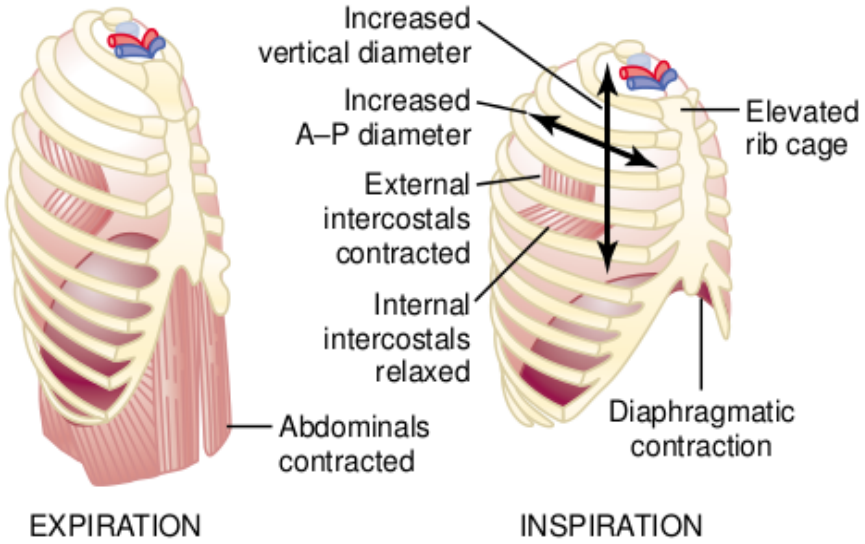


Figure 1.9 - Dynamics of breathing

During inspiration the rise of the ribcage is realized by the external and parasternal intercostals muscles, and this in association with the contraction of the diaphragm allows the lungs to expand more in the chest wall.

In expiration instead the accessory respiration muscles – the *sternocleidomastoid muscles,*

the anterior serrati, and the scaleni – acts lifting upward on the sternum and elevating the first ribs.

The lung compression is realized by the contraction of the internal intercostal muscles, that lower the ribs; and by the abdominal muscles which pushes the abdomen upward against the bottom of the diaphragm, thereby compressing the lungs.

1.3.2 Air diffusion

Oxygen and carbon dioxide move between air and blood by simple diffusion.

In the process of diffusion, gas flows between air and blood occurs passively driven by their partial pressure gradients.

The partial pressure of each gas in the alveolar respiratory gas mixture tends to force molecules of that gas into solution in the blood of the alveolar capillaries and vice versa.

At alveolar level partial pressure of respiratory gases are not the same of the ones in atmospheric air: an overview of partial pressures of respiratory gases during respiration cycle is described in Fig. 1.10.

Partial Pressures of Respiratory Gases as They Enter and Leave the Lungs (at Sea Level)

	Atmospheric Air* (mm Hg)		Humidified Air (mm Hg)		Alveolar Air (mm Hg)		Expired Air (mm Hg)	
N_2	597.0	(78.62%)	563.4	(74.09%)	569.0	(74.9%)	566.0	(74.5%)
O_2	159.0	(20.84%)	149.3	(19.67%)	104.0	(13.6%)	120.0	(15.7%)
CO_2	0.3	(0.04%)	0.3	(0.04%)	40.0	(5.3%)	27.0	(3.6%)
H_2O	3.7	(0.50%)	47.0	(6.20%)	47.0	(6.2%)	47.0	(6.2%)
TOTAL	760.0	(100.0%)	760.0	(100.0%)	760.0	(100.0%)	760.0	(100.0%)

Figure 1.10 - Partial Pressures of Respiratory gases as they enter and leave the lungs

The gas exchange occurs at the contact zone between the alveolus and the pulmonary capillary: gas molecules dissolve into tissues passing through alveolar and blood vessels membranes and epithelium.

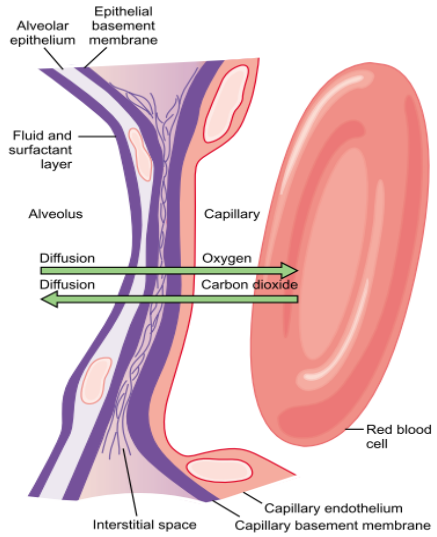


Figure 1.11 - Gas diffusion from alveoli to blood

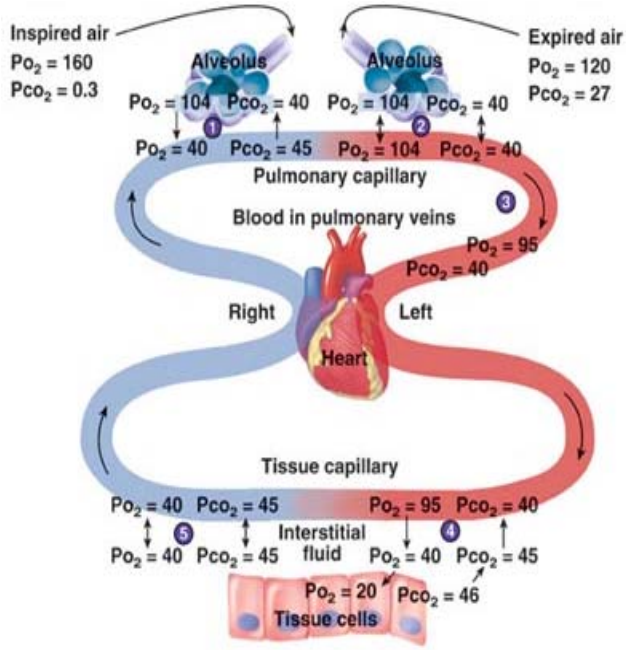


Figure 1.12 - Partial pressures values from alveoli to tissues

Figure 1.12 shows the partial pressures of respiratory gasses at different stages from alveoli

to tissues. Giving attention to the oxygen diffusion process, it can be seen that the Po2 alveolus averages 104 mm Hg, whereas the Po2 of the gaseous oxygen in the of the venous blood entering the pulmonary capillary at its arterial end averages only 40 mm Hg because a large amount of oxygen was removed from this blood as it passed through the peripheral tissues.

Therefore, the initial pressure difference that causes oxygen to diffuse into the pulmonary capillary is 104 – 40, or 64 mm Hg.

When the arterial blood reaches the peripheral tissues, its Po2 rounds the tissue cells averages only 40 mm Hg. Thus, the pressure difference causes again oxygen to diffuse rapidly from the capillary to cells.

The mechanisms of diffusion of CO_2 are driven by gradient of pressure, such the one of the oxygen; but ruled by a different diffusion coefficient.

The diffusion coefficient is proportional to solubility of the gas and inversely proportional to the square root of the molecular weight. This means that CO2, diffuses about 20 times more rapidly than does O2 through tissue sheets because it has a much higher solubility but not a very different molecular weight.

Because of low solubility the oxygen dissolved in blood is almost about low concentrated – only 10^{-4} [6], and the oxygen flow that arterial blood provides represents only 5% of total amount necessary for metabolic consumption[6].

To have the right amount needed for metabolism, oxygen indeed, is carried through blood in two different ways: by the dissolution in plasma and by the binding with *hemoglobin* contained in red blood cells.

Hemoglobin is metalloprotein, able to bind molecules of O2 within alveolar capillaries and to carry them to tissues: it can also transport carbon dioxide from peripheral organs from tissues to lungs [6].

Figure 1.13 shows hemoglobine dissociation curve on partial pressure of O2.

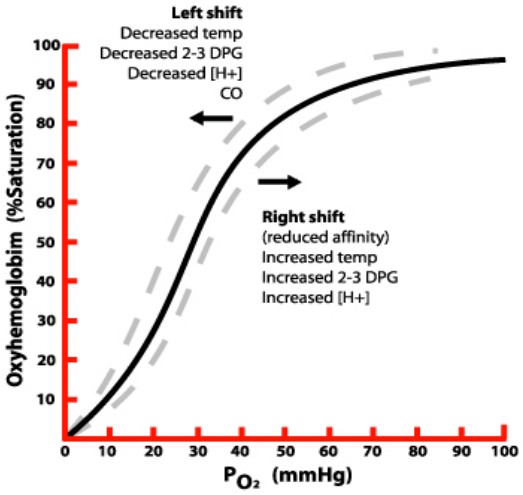


Figure 1.13 - Hemoglobine dissociation curve: At 100% of saturation, 1 g of hemoglobin bind 1,34-1,39 ml of oxygen: if in the blood there were 15 g of hemoglobin for 100 ml of blood, in arterial blood there can be carried 20ml of O2 on 100 ml of blood [6]

Oxygen partial pressure regulates *hemoglobin saturation*, which is the amount of oxygen, can be bound to hemoglobin at a specific concentration.

When Po2 is high, as in the pulmonary capillaries, oxygen binds with the hemoglobin, but when Po2 is low, as in the tissue capillaries, oxygen is released from the hemoglobin: this allows the oxygen diffusion in cells.

Thus, the uptake of oxygen can be summarized in the following stages: oxygen diffuses from alveoli through blood because of the difference in partial pressures, and depending on this oxygen binds with hemoglobine since the equilibrium between the oxygen dissolved and oxygen bound is reached.

The hemoglobin dissociation curve can be described by the Hill equation [10].

Assuming that the molecules of Hb might aggregate differently because of the various salts present in solution, and thus different aggregates of Hb might co-exist in the same solution, several simultaneous equilibrium reactions between oxygen and Hb might coexist as well.

If a solution would contain only Hb and Hb_n (an aggregate of n molecules of Hb), the equilibrium reaction would be:

$$Hb+O2 \text{—>} HbO2 \qquad [1.2]$$

$$Hb_n + nO2 \text{—>} Hb_nO2_n$$

In the special case of a solution with only Hb and Hb2, the equation of the dissociation curve of Hb proposed by Hill is:

$$y2 = \frac{\lambda K_2}{\left(1 + K_2 x^2\right)} + \frac{\left(100 - \lambda\right) K_1 x}{\left(1 + K_1 x\right)} \qquad [1.3]$$

where *y2* is the percent saturation of Hb, *x* is the partial pressure of O2 (mmHg), λ is the percentage of Hb2, and (100 -λ) is the percentage of Hb. K1 and K2 were called by Hill the 'equilibrium constants' of the equilibrium reactions [10].

As can be seen on (1.3) the Hill equation mathematically shows the dependence of saturation on oxygen partial pressure: typically there are other several factors related to blood composition that influences hemoglobin oxygen-binding capacity, such increased carbon dioxide partial pressure and consequential changes in blood pH (acidosis and Bohr effect)[6], temperature and increased 2,3-biphosphoglycerate (BPG), a metabolically important phosphate compound present in the blood in different concentrations under different metabolic conditions[5].

This dependence graphically reflects in a shift of the dissociation curve (Figure 1.12).

According to the Hill equation, the measurement of partial pressure of oxygen dissolved on blood can be considered an indirect estimation of the percent saturation of hemoglobin and at last can be a useful indicator of to gas exchange between the alveoli and blood, and of oxygenation of the tissues in pathological and physiological conditions.

1.3.3 Mechanics of respiration

The study of mechanics of respiration is a useful approach to have information on the physiological state of the respiratory system in normal and pathological conditions.

Essentially, this means to describe the statics and the dynamics of the whole and of each component of the apparatus.

Because the respiratory system and its parts have tridimentional geometry, get information about the dynamical and the statical variables, such as positions, displacements and forces means to measure volumes and pressures variation.

1.3.1.1 Lung volumes

In describing the events of pulmonary ventilation, the volume of air engaged in the respiration act is conventionally subdivided into four *volumes* and four *capacities* [4]. The last are a combination of two or more of the first and both are defined as follow:

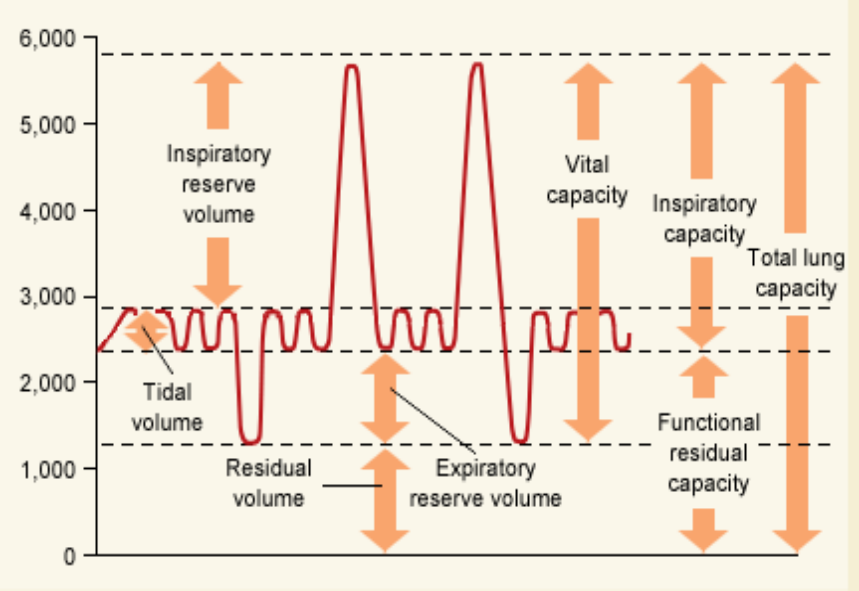


Figure 1.14 - Lung Volumes

- *the tidal volume* is the volume of air inspired or expired with each normal breath.
- *the inspiratory reserve volume* is the extra volume of air that can be inspired over and above the normal tidal volume when the person inspires with full force
- *the expiratory reserve volume* is the maximum extra volume of air that can be expired by forceful expiration after the end of a normal tidal expiration
- *the residual volume* is the volume of air remaining in the lungs after the most forceful expiration
- *the inspiratory capacity* equals the tidal volume plus the inspiratory reserve volume. This is the amount of air a person can breathe in, beginning at the normal expiratory level and distending the lungs to the maximum amount.
- *the functional residual capacity equals* the expiratory reserve volume plus the residual volume. This is the amount of air that remains in the lungs at the end of normal expiration.
- *the vital capacity* equals the inspiratory reserve volume plus the tidal volume plus

the expiratory reserve volume. This is the maximum amount of air a person can expel from the lungs after first filling the lungs to their maximum extent and then expiring to the maximum extent.

- the *total lung capacity* is the maximum volume to which the lungs can be expanded with the greatest possible effort; it is equal to the vital capacity plus the residual volume

It's important to notice that the measures of pulmonar volumes are of two types:

- *absolutes:* such as total lung capacity (TLC), functional residual(FRC) and residual volume (RV)
- *relatives*: such as tidal volume. vital capacity, the inspiratory and expiratory reserve volumes and the inspiratory capacity

Relative measures of pulmonary volumes can be easily obtained by the integration of measures of the respiratory flow, conversely to the absolute ones that need more complex measurement protocol to be got.

Another way to obtain information about respiratory volumes is through *pletismography,* or rather the measure of the volume variation of the chest wall [10].

Pletismography can be realized in different modalities: the one used in this work is described in Chapter 3.

1.3.1.2 Pressures

It has been previously shown how respiratory muscles act as a respiratory pump.

The measures of pressure considered to describe the behaviour of such a pump, and thus of the mechanics of the respiratory system are typically the following ones:

- P_{bs} *(body surface)* is the external pressure of the chest wall, in normal conditions it is worth the same value of the atmospheric pressure.
- P_{pl} *(pleural)* is the pleural fluid pressure, in normal conditions it is worth less than the atmospheric pressure. It is not directly measured, perforating the membrane, but it is estimated from oesophageal pressure, introducing a catheter with a balloon in the oesophagus, which position is nearby the pleura.
- P_{alv} *(alveolar)* is the pressure into the alveoli.
- P_{ao} *(airway opening)* is the pressure at the entrance of airways (mouth), and it is the same of Palv if there are no pressure drops along the ducts.

- P_l *(lung)* is the pressure at which the lung is subjected and it is called distension pressure (elastic pressure). Mathematically, it is the difference between alveolar and pleural pressures: Pl=Palv-Ppl. If Pl increases, the lung expands.
- P_w *(wall)* is the pressure at which the chest wall is subjected t, and it is worth the difference between pleural and extern pressures: Pw=Ppl-Pbs.
- P_{rs} *(respiratory system)* is the pressure at which is subjected the respiratory system, and it is worth the sum between pulmonary and wall pressures, hence the difference between alveolar and extern pressures: Prs=Pl+Pw=(Palv-Ppl)+(Ppl-Pbs)=Palv-Pbs (in static conditions)

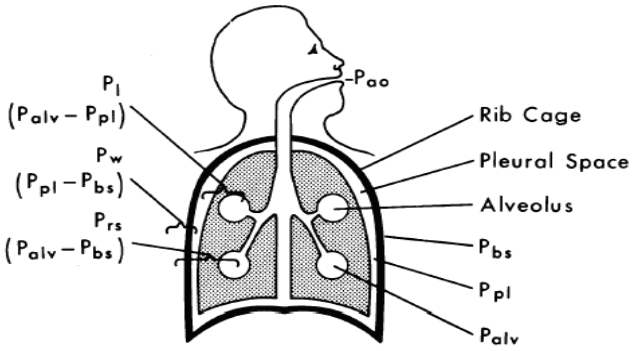


Figure 1.15 - Pressures within the respiratory system

1.3.1.3 Pressure-Volume curve in static conditions

Information on the mechanical behaviour of the respiratory system during breathing in health and disease can be gained analysing the pressure volume curve in static condition.
The static pressure-volume (P-V) curve (Figure 1.16) of the respiratory system describes the mechanical behaviour of the lungs and chest in conditions of constant air flow [12].
Such condition, during quite breathing, exists only at the end of an inspiration or expiration, when the air flow stops.

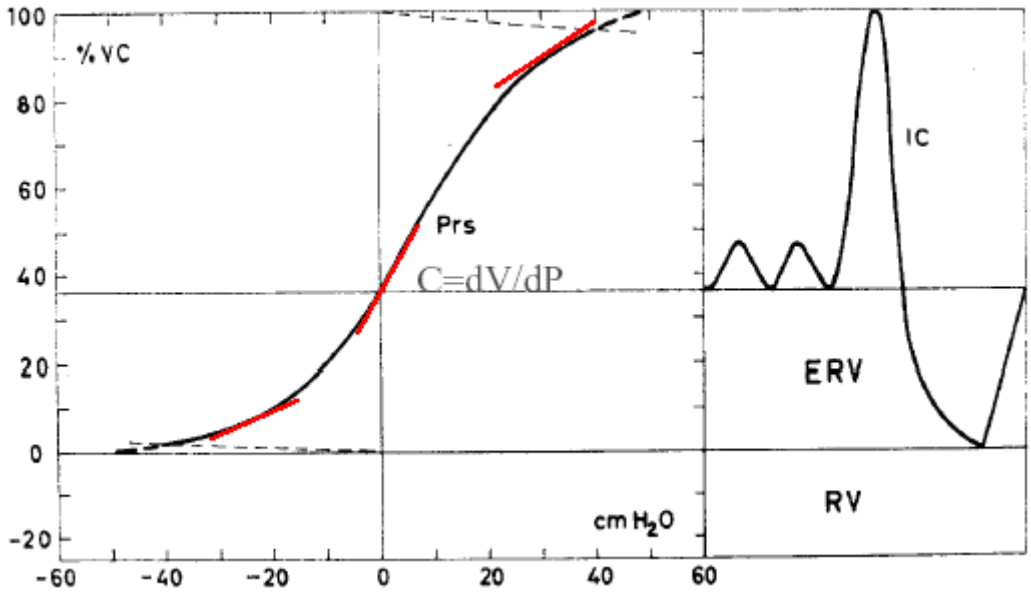


Figure 1.16 Pressure-volume curve in static condition: on the abscissa there is respiratory system pressure P_{rs} in cmH_2O, on the ordinate there is lung volume expressed as percentage of vital capacity (residual volume is considered the zero).

The shape of the curve in an upright, awake, and relaxed subject is sigmoidal, with upward concavity at low inflation pressure and downward concavity at higher inflation pressure: that sigmoidal shape reflects the balance between the expansive force of the chest wall (diaphragm and rib cage) and the inward retractile force of the elastic recoil of lung parenchyma [12].

The slope of the curve represents the compliance of the respiratory system and its expression is:

$$C = dV / dP \qquad [1.4]$$

The compliance of a system expresses how easily it distends: high compliance is related at high distensibility and this occurs when the system is rather stretchable.

At the lower end of the curve (low lung volume), the compliance is low, which means that there is a small change in volume for a large change in pressure: this region is below *critical opening pressure,* the threshold to prevent terminal airways and alveoli collapse, thus in that case extra-pressure is required to open them [15].

At the center of the curve the compliance increases resulting in a large change in volume for a small change in pressure.

This is where normal tidal breathing should occur because efficiency is maximal.

At the upper end of the curve (high lung volume), the compliance decreases again and the lungs gets stiffer: at high expanding pressures, in fact, the lung is over inflated and oppose to further volume increases.

Out of normal conditions, low compliance indicates a stiff lung and means extra work is required to bring in a normal volume of air: this occurs as the lungs in this case become fibrotic, lose their distensibility and become stiffer.

In a highly compliant lung, indeed, as in emphysema, the elastic tissue has been damaged. Patients with emphysema have very high lung compliance due to the poor elastic recoil; they have no problem inflating the lungs but have extreme difficulty exhaling air. In this condition extra work is required to get air out of the lungs.

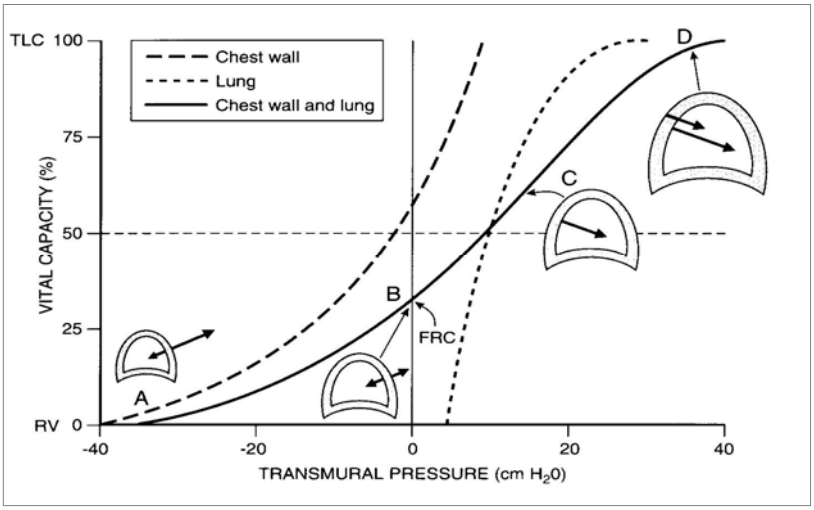


Figure 1.17 - The relaxation static pressure-volume curve of the lung, chest wall, and respiratory system in setting posture.The curve for the respiratory system is the sum of the individual curves.The horizontal distance from the curve to the zeropressure axes indicates the pressure exerted by the passive structure of the system at a givenvolume.

The pressure-volume curve of the respiratory system (RS) is given by the sum of the pressure-volume graphs of the lungs (L) and of the chest wall (CW).

$$P_L = P_l = P_{alv} - P_{pl} \quad [1.5]$$

$$P_W = P_w = P_{pl} - P_{bs} \quad [1.6]$$

$$P_{rs} = P_l + P_w = P_{alv} - P_{bs} \quad [1.7]$$

The chest wall contributes most to the curvature below FRC, and the lung contributes most to the curvature above FRC (Figure 1.17).

The lung curve is determined by the characteristic of the parenchyma, the curve of the chest wall derives from the passive behaviour of the tissue that constructs the chest and all organs which somehow interferes with lung movements, while the respiratory system curve is, at every volume, the combination of this two components.

At *resting volume,* volume corresponding at zero pressure of the respiratory system (FRC) the chest wall recoils outward (its transmural pressure at this volume is subatmospheric) with a pressure equal to that by which the lung recoils inward (its transmural pressure at this volume is greater than atmospheric pressure).

At zero pressure the lung is at its minimal volume, which is below RV.

Considering the chest wall alone, indeed, the pressure is negative at low volumes and FRC becomes positive when the volume is increased at approximately 60% of the VC: below this volume the chest wall tends to recoil outward.

At TLC, both the lung and chest wall pressures are positive, and they both require positive transmural distending pressures. During inspiration at volumes greater than 60% of VC, both systems tend to recoil inward, therefore muscular work is necessary to oppose to this tendency and to expand the thorax.

During expiration, the system (chest wall + lung) returns the elastic energy, stored during inspiration, coming back to its resting value.

Thus, the lung and the chest wall behave like two opposing springs in series.

Considering that also the ribcage is an elastic structure as the lung, the elastic energy released by the collapsing tendency of the lungs is balanced by the expanding tendency of the chest wall.

Thus is can be considered the total system compliance as:

$$\frac{1}{C_{RS}} = \frac{1}{C_L} + \frac{1}{C_{CW}} \qquad [1.8]$$

in which CRS is the compliance of the total respiratory system, CL is the compliance of the lung, and CCW is the compliance of the chest wall.

The role of surfactant

Two components contribute to lung elastic recoil. The first is tissue elasticity (1/3 of the total elastic forces); the second is related to the forces needed to change the shape of the air-liquid interface of the alveolus (2/3 of the total elastic forces).

Expanding the lungs requires overcoming local surface forces that are directly proportionate to the local surface tension of the liquid film covering the alveoli.

The law of Laplace quantifies this force:

$$P = 2T / R \quad [1.9]$$

The pressure needed to keep open the alveoli is directly proportionate to the surface tension at the interface and inversely proportionate to the radius of the alveoli (Figure 1.18).

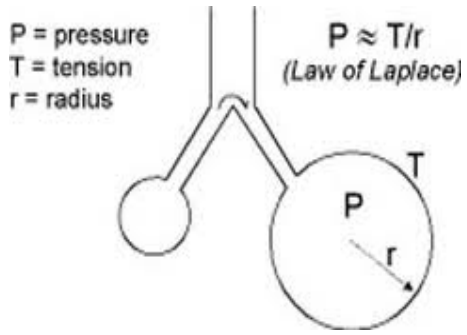


Figure 1.18 - Laplace law applied to a spherical alveolus covered by a liquid film

The liquid film that covers the alveoli is called, surfactant and is a mixture of phospholipids and proteins [6]. These hydrophobic molecules displace water molecules from the air-liquid interface, thereby reducing surface tension.

This reduction has three physiologic implications: First, it reduces the elastic recoil pressure of the lungs, thereby reducing the pressure needed to inflate them. This results in reduced work of breathing. Second, it allows surface forces to vary with alveolar surface area, thereby promoting alveolar stability and protecting against collapsing. Third, it limits the reduction of hydrostatic pressure in the pericapillary interstitium caused by surface tension [6].

Pathologic states may result from changes in lung elastic recoil related to an increase in compliance, as in emphysema, a decrease in compliance, as pulmonary fibrosis, or a disruption of surfactant with an increase in surface forces [5].

Hysteresis of the lung

An important phenomenon that is readily seen in P-V curves is *hysteresis.*

Hysteresis refers to unrecoverable energy, or delayed recovery of energy, that is applied to a system.

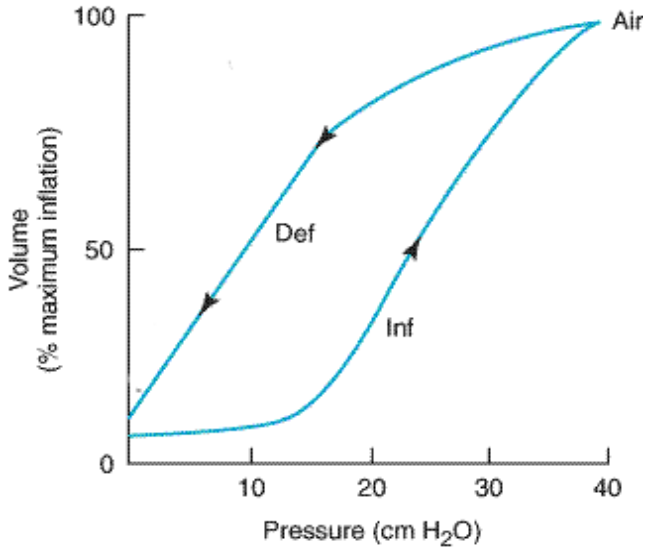


Figure 1.19 - V-P curve during inflation (inf) and deflation(def)

The V–P curve during lung deflation is not the same as during lung inflation, reflecting static hysteresis (Figure 1.19).

That is, the lung does not act as a perfect elastic system, in which any energy put in is immediately returned.

This may involve three main mechanisms: plastic behaviour of tissue elements and true tissue hysteresis; surface hysteresis; and differences in the sequence of recruitment and derecruitment of lung units between inflation and deflation [1].

1.3.1.4 The electrical model of the respiratory system

The mechanics of the respiratory system can be described using an analogous electrical model constituted by the series of airways (AW), lungs (L) and chest wall (CW).

The term corresponding to the current is the flow, while the voltage is the electrical analogous of the pressure.

The airways cause a pressure drop of Pao-Palv, the lungs cause a pressure drop of Palv-Ppl and the chest wall cause a pressure drop of Ppl-Pbs.

In the alveoli there are air compression and expansion phenomena, which are considered in the model with a capacitance.

The ventilatory pump acted by respiratory muscles can be modelled as a voltage generator (MUS) representing the pressure generated by the muscles; the generator acts on the pleural

pressure through the chest wall: when it decreases the pressure there is the inspiration, when it increases the pressure the expiration happens.

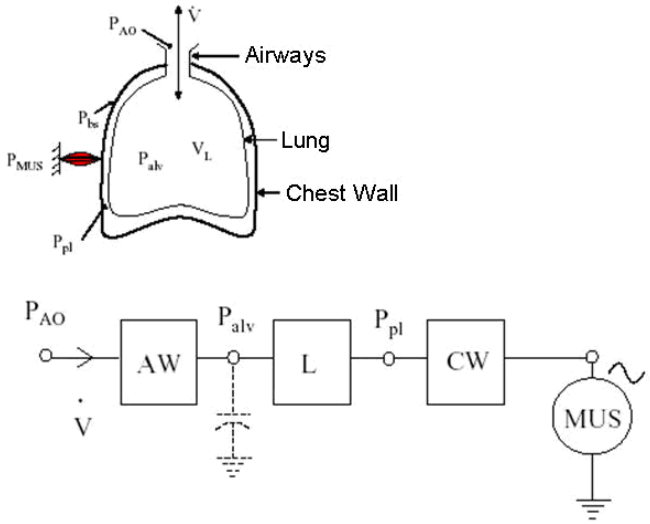


Figure 1.20 - Airways model with muscles as active generator.

1.3.4 Nervous control of respiration

Breathing is under the control of the nervous system that normally adjusts rhythmic ventilatory pattern in order to handle the demands of the body of oxygen.

Cycle rhythm of breathing is mainly generated by groups of neurons located bilaterally in the medulla oblongata and pons of the brain stem (Figure 1.21) [3].

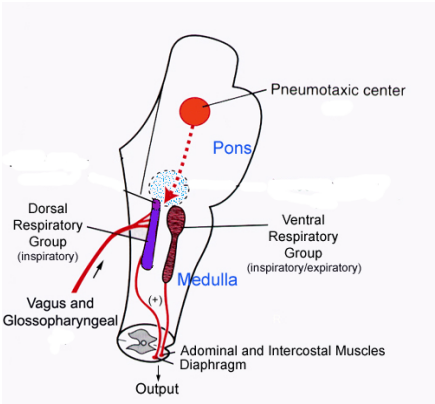


Figure 1.21 - Central Controller of respiratory system: they are the dorsal respiratory group (DRG), which mainly causes inspiration a ventral respiratory group, the ventral respiratory group (VRG), involved both in inspiration and expiration and the pneumotaxic center or pontine neurons,which mainly controls rate and depth of breathing

The basic cycle of respiration is highly modified by several control mechanism and by voluntary efforts: their interaction provides a large capacity and flexibility to the respiratory system at the more diverse conditions.

Basically, respiration control is carried out with the regulation of the frequency and tidal volume during breathing in order to maintain the partial pressure of arterial oxygen and carbon dioxide within a narrow range, despite fluctuations in oxygen consumption, carbon dioxide production, and changes in metabolic demand [13].

Normal respiration maintains blood gas and acid-base homoeostasis within strict levels with minimal expenditure of mechanical energy.

This homeostatic control system relies on three components:

1. *Sensors*, which gather information and feed it to the central nervous system, they are
    - *peripheral chemoreceptors,* located in the carotid and aortic bodies, peripheral chemoreceptors are responsive to changes in PaO_2, $PaCO_2$ and pH. Those receptors are strongly linked to the cardiovascular function. Respiratory cessation and circulatory shock increase chemoreceptor activity, enhancing sympathetic outflow to the heart and vasculature via activation of the vasomotor center[14].
    - *central chemoreceptors* on the ventral surface of the medulla oblongata, in direct contact with cerebrospinal fluid, senses changes in hydrogen ion and carbon dioxide concentrations.
    - *stretch receptors of the lungs* and *chest-wall and muscle mechanoreceptors,* the firsts monitor the lung stretching, to prevent overinflation: when this occurs they signal the respiratory centers to exhale and inhibit inspiration. The seconds respond to changes in length, tension or movement of the respiratory muscles.
    - *irritants receptors*: locate in the airways they sense the presence of toxic substances in the airways, their signals the respiratory causes the contraction of the respiratory muscles, causing coughing and sneezing.
2. *Central controller* consists of the neuron of the brainstem group, that realize involuntary control and the cerebral cortex structures that are involved in voluntary control.
3. *Effectors*, which is the respiratory muscles.

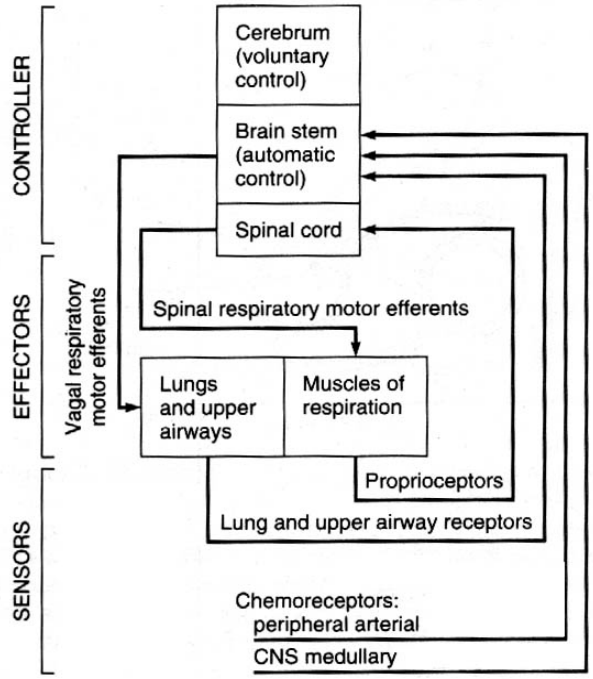


Figure 1.22- Schematic representation of the Nervous Respiratory control system

This structure realized a negative feedback control system.

This feedback can be modulated by higher cortical centres, realizing the voluntary control effort.

Abnormal conditions stimulate the system action that modifies the ventilation pattern in order in respond to variations from the homeostatic state [2].

1.4 Respiratory disorders

1.4.1 Chronic obstructive pulmonary disease (COPD)

Chronic obstructive pulmonary disease (COPD) is a disease state characterized by poorly reversible airflow limitation that is not is usually progressive and associated with an abnormal inflammatory response of the lungs [41]. COPD is currently the fourth leading cause of death in the world, and further increases in the prevalence and mortality of the disease can be predicted in the coming decades [44, 57, and 58]. The prevalence of COPD in the general population is estimated to be, 1% across all ages rising steeply to 10% amongst those aged 40 years the prevalence climbs appreciably higher with age [58] and between smokers [49]. The chronic airflow limitation characteristic of COPD is caused by the structural changes occurring with inflammation of the central and peripheral airways, lung parenchyma, and pulmonary vessels: these include inflammation of the peripheral airways, which characterizes *obstructive bronchiolitis;* parenchymal destruction, which characterises *emphysema;* and inflammation of the central airways, which characterizes *chronic bronchitis* [41].

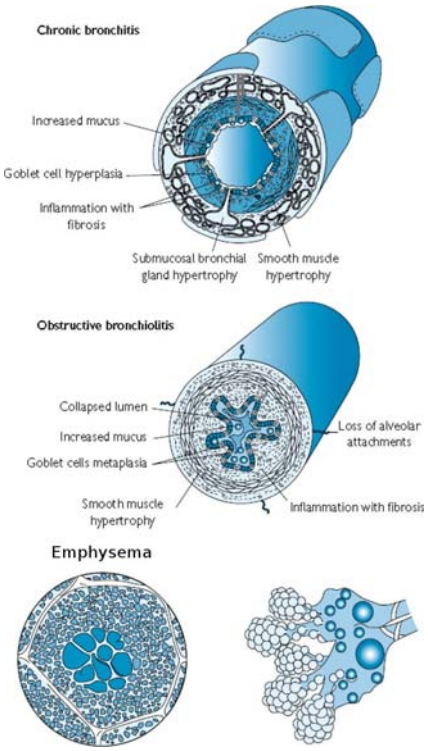


Figure 1.23 - Anatomopathological representation of Chronic bronchitis, Obstructive bronchitis and Emphysema

The distinctive feature of chronic bronchitis is hypersecretion of mucus, beginning in the central airways, the trachea, bronchi, and bronchioles greater than 2 to 4 mm of internal diameter.

Irritants (cigarette smoke and pollutants) induce hypersecretion of the bronchial mucous glands, cause hypertrophy of mucous glands, and lead to metaplastic formation of mucin-secreting goblet cells in the surface epithelium of bronchi. In addition, they cause inflammation with infiltration of CD8+ T cells, macrophages, and neutrophils.

In the peripheral airways—small bronchi and bronchioles that have an internal diameter of less than 2 mm— chronic inflammation leads to repeated cycles of injury and repair of the airway wall .

The repair process results in a structural remodelling of the airway wall, with increasing collagen content and fibrosis that narrows the lumen and produces fixed airways obstruction.

Destruction of the lung parenchyma in COPD typically occurs as centrilobular emphysema [46, 47], beginning in and around the centres of the pulmonary lobules.

Emphysema is seen to be the result of the action of the mechanical forces exerted by air trapped beyond obstructed bronchioles (Figure 1.24) [45].

This action leads to the break of alveolar attached to the small airways and decreases lung elastic recoil; in turn, these changes diminish the ability of the airways to remain open during expiration [41].

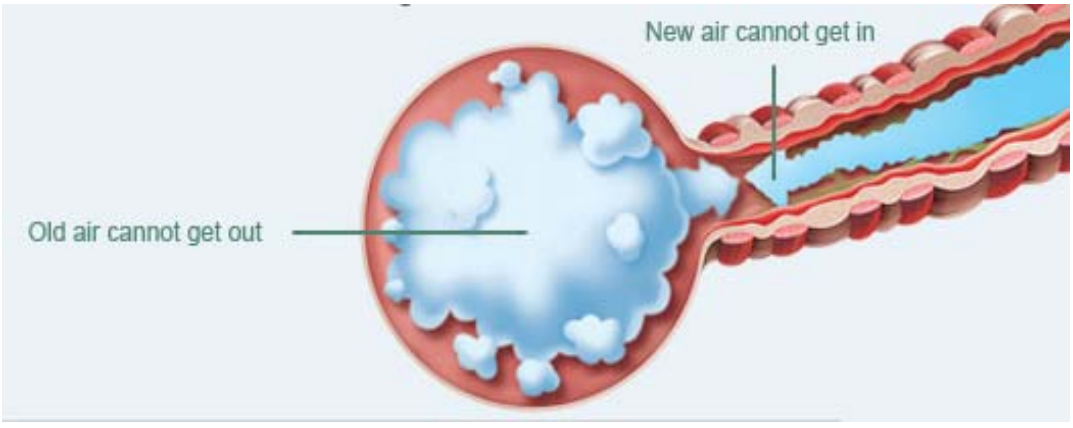


Figure 1.24 - Obstructed Bronchioles and air trapping mechanism

COPD is a polygenic disease and a classic example of gene-environment interaction. The genetic risk factor that is best documented is a severe hereditary deficiency of alpha-1 antitrypsin, a major a major circulating inhibitor of serine proteases [63].

Gene activation and disease development are common attributed to long-term exposure to toxic gases and particles.

Smoking is the best studied COPD risk factor, it is not the only one and there is consistent evidence from epidemiologic studies that non-smokers may develop chronic airflow obstruction.

Because individuals may be exposed to a variety of different types of inhaled particles over their lifetime, it is helpful to think in terms of the total burden of inhaled particles. Each type of particle, depending on its size and composition, may contribute a different weight to the risk, and the total risk will depend on the integral of the inhaled exposures [41].

The irritation and damage that cause COPD thus, can have several possible causes, including:

Tobacco Smoke: Cigarette smoking is by far the most commonly encountered risk factor for COPD. Cigarette smokers have a higher prevalence of respiratory symptoms and lung function abnormalities, a greater annual rate of decline in FEV1, and a greater COPD mortality rate than non-smokers. The risk for COPD in smokers is dose-related. Age at starting to smoke, total pack years smoked, and current smoking status are predictive of COPD mortality. Not all smokers develop clinically significant COPD, which suggests that genetic factors must modify each individual's risk [64].

Second hand smoke: Passive exposure to cigarette smoke may also contribute to respiratory symptoms and COPD by increasing the lungs' total burden of inhaled particulates and gases [65].

Occupational Dusts and Chemicals: Occupational exposures are an underappreciated risk factor for COPD. These exposures include organic and inorganic dusts infections. These exposures can lead to chronic COPD or can cause acute COPD episodes, called *exacerbations*, in people whose COPD is under control.

Indoor air pollution: wood, animal dung, crop residues, and coal, typically burned in open fires or poorly functioning stoves, may lead to very high levels of indoor air pollution. Almost 3 billion people worldwide use biomass and coal as their main source of energy for cooking, heating, and other household needs, so the population at risk worldwide is very

large. In these communities, indoor air pollution is responsible for a greater fraction of COPD risk than SO2 or particulates from motor vehicle emissions [66].

Outdoor Air pollution: High levels of urban air pollution are harmful to persons with existing heart or lung disease. The role of outdoor air pollution in causing COPD is unclear, but appears to be small when compared with that of cigarette smoking. It has also been difficult to assess the effects of single pollutants in long-term exposure t o atmospheric pollution. However, air pollution from fossil fuel combustion, primarily from motor vehicle emissions in cities, is associated with decrements of respiratory function. The relative effects of short-term, high peak exposures and long-term, low-level exposures are a question yet to be resolved [68].

Infections: infections (viral and bacterial) may contribute to the pathogenesis and progression of COPD, and the bacterial colonization associated with airway inflammation50, and may also play a significant role in exacerbations. A history of severe childhood respiratory infection has been associated with reduced lung function and increased respiratory symptoms in adulthood[70]

However, viral infections may be related to another factor, e.g., low birth weight, that itself is related to COPD [71].

Oxidative stress: The lungs are continuously exposed to oxidants generated either endogenously from phagocytes and other cell types or exogenously from air pollutants or cigarette smoke. In addition, intracellular oxidants, such as those derived from mitochondrial electron transport, are involved in many cellular signalling pathways. Lung cells are protected against this oxidative challenge by well developed enzymatic and nonenzymatic systems. When the balance between oxidants and antioxidants shifts in favour of the former depletion of antioxidants oxidative stress occurs. Oxidative stress not only produces direct injurious effects in the lungs but also activates molecular mechanisms that initiate lung inflammation. Thus, an imbalance between oxidants and antioxidants is considered to play a role in though pathogenesis of COPD [72].

1.4.1.1 Diagnosis and classification of severity

According to guidelines, COPD should be suspected in any patient aged 40 years or more with symptoms of cough, sputum production, or breathlessness and/or a history of exposure to risk factors, in particular smoking [41].

Defining the *forced expiratory volume* (FEV_1)as the volume expired in a one-second forced exhalation measured in litres; the presence of a FEV1<80% of the predicted value performed after the administration of an adequate dose of an inhaled bronchodilator (e.g., 400 μg salbutamol) in combination with an FEV_1 /FVC<70% confirms the presence of airflow limitation that is not fully reversible [45].

The impact of COPD on an individual patient depends not just on the degree of airflow limitation, but also on the severity of the symptoms: these are chronic and progressive and their identification may prevent the risk of further exacerbation of the disease.

The classification of severity of COPD now includes four stages classified by the level of airflow limitation (measured by spirometric indexes) and the occurrence of symptoms [41]:

- *Stage 0: At Risk* - characterized by chronic cough and sputum production. Lung function, as measured by spirometry, is still normal
- *Stage I: Mild COPD* - characterized by mild airflow limitation (FEV1/FVC < 0.70; FEV1 ≥ 80 % predicted). Symptoms of chronic cough and sputum production may be present, but not always. At this stage, the individual is usually unaware that his or her lung function is abnormal.
- *Stage II: Moderate COPD* - characterized by worsening airflow limitation (FEV1/FVC < 0.70; 50% ≤ FEV 1 < 80% predicted), with shortness of breath typically developing on exertion and cough and sputum production sometimes also present. This is the stage at which patients typically seek medical attention because of chronic respiratory symptoms or an exacerbation of their disease.
- *Stage III: Severe COPD* - characterized by further worsening of airflow limitation (FEV1/FVC < 0.70; 30%≤ FEV1 < 50% predicted), greater shortness of breath, reduced exercise capacity, fatigue, and repeated exacerbations that almost always have an impact on patients' quality of life.
- *Stage IV: Very Severe COPD* - characterized by severe airflow limitation (FEV1/FVC < 0.70; FEV1 < 30% predicted or FEV1 < 50% predicted plus the presence of chronic respiratory failure). Respiratory failure is defined as an arterial partial pressure of O2 (PaO2) less than 8.0 kPa (60 mm Hg), with or without arterial partial pressure of CO2 (PaCO2) greater than 6.7 kPa (50 mm Hg) while breathing air at sea level.

1.4.1.2 Pathophysiological effects of COPD: Lung hyperinflation and chest-wall asynchronies

The structural changes occurring with inflammation and emphysema in COPD subjects result also in changes of the mechanical properties of the airways and the lungs.

The characteristics modifications consists of a increase in static compliance (the lung is more distensible), a reduction of the static transpulmonary pressure at a given volume, a increases in airway resistance and loss of lung recoil that lead to hyperinflation of the lungs and chest-wall and greatly increase the work of breathing[52].

Lung hyperinflation is present when gas volume in the lungs, or in a region of the lung, is increased compared with the predicted value [50].

Lung hyperinflation is a common finding in COPD and causes inspiratory muscle shortening and weakening, particular the diaphragm, reducing its capability to generate pressure and displace volumes.

In healthy people, inspiration occurs as a result of the coordinated action of the chest wall muscles and diaphragm. As the diaphragm flattens, the incompressible abdominal contents displace the abdominal wall outwards

During inspiration, the expansions of the abdomen and both ribcage compartments are in phase.

In patient with COPD and hyperinflation , the diaphragm is flatter and lower than in normal subjects is flatter and lower than in normal subjects and the zone of apposition (the part of the diaphragm witch faces the lower part of the rib cage) is lower in size[52].

In this condition, the contraction of the diaphragm no longer increase lung volume or expand the abdomen, and it produces an inspiratory decrease in the transverse diameter of the lower rib cage [55].

This makes inefficient the translation of pressure generated by the diaphragm to the lower part of the ribcage [53]

In Figure 1.25 is reported a study of Martinez et al.[56] on the ongoing of inspiratory pressure generation during tidal breathing in n 45 patients affected by CODP with varying degrees of airflow obstruction and hyperinflation.

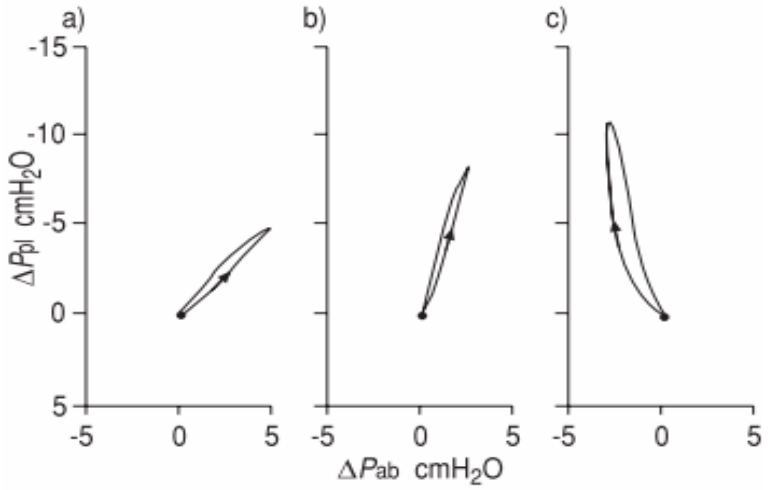


Figure 1.25 - Inspiratory pressure generation during tidal breathing: a) in a normal subject; b) in a patient with moderately severe chronic obstructive pulmonary disease (COPD); and c) in a patient with severe COPD. The pleural pressure swing (ΔPpl) is on the ordinate, and the abdominal pressure swing (ΔPab) is on the abscissa [56].

The closed circle in each panel corresponds to end-expiration, and the arrow marks the inspiratory phase of the breathing cycle. In the normal subject (a), Pab increases during inspiration by about as much as Ppl decreases. However, in the patient with moderately severe COPD (b) , ΔPpl is greater but ΔPab is smaller. The patient with severe COPD (c) may have a decrease in Pab during inspiration, which corresponds to a downward displacement of the diaphragm and an inward displacement of the ventral abdominal wall.

This phenomenon inevitably causes a decrease in tidal volume because the inspiratory motion of one compartment is opposed by the expiratory action of the other compartment [54].

Externally it can be seen as paradoxical inward movement during inspiration, which reflects the chest-wall asynchronous movement respect abdomen.

This pattern is typical in adult COPD patient and is also known as *Hoover' sign* [52]

More precise quantification of the chest-wall asynchronies can be observed through respiratory inductance plethysmography (RIP) using two elastic inductance coil sensors to the respiratory excursion of the ribcage (RC) and abdomen ABD.

Chest-wall asynchronies can be detected, quantified and monitored objectively by calculating the phase shift between the RC and AB signals through the phase angle analysis of the Lissajous figures utilizing the method of Agostoni and Mognoni.[62].

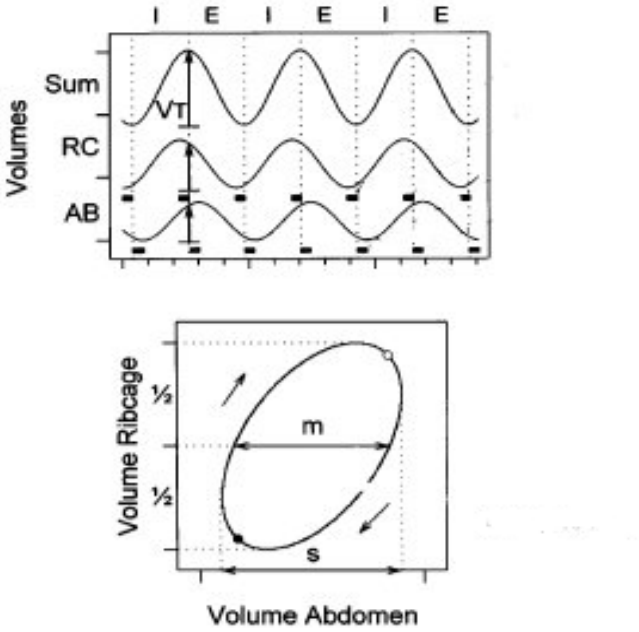


Figure 1.26 - Representation of RIP recording as time series and in the Lissajous figures in inspiration (open loop) RC=Ribcage Volume, AB=Abdomen Volume, Sum=RC+AB, V_T=tidal volume

Implicit in this technique is the assumption the both the RC and AB signals are sinusoidal, and simply shifted relative to one another.

RIP recordings are schematically visualized by time series plots of rib cage (RC) and abdominal (AB) volumes along with their sum (Sum).

End-expiration and end-inspiration are marked by a *closed circle* and an *open circle*, respectively.

Tidal volumes (V_T inspiratory amplitude of sum signal) and the duration of inspiratory (I) and expiratory (E) phases of the breathing cycles are derived from the sum signal

The phase angle (PhAng) between rib cage and abdominal wave-forms is derived from the ratio[61]:

$$\sin(PhAng) = m / s \qquad [1.10]$$

where *m* is the line parallel to the abscissa on the RC-AB plot at 50% the distance between the maximal RC (half rib-cage tidal volume Konno et Al.[51]) perpendicular intercept and

the origin, and s is the length of a line from the maximal AB (abdominal tidal volume) perpendicular intercept minus the origin.

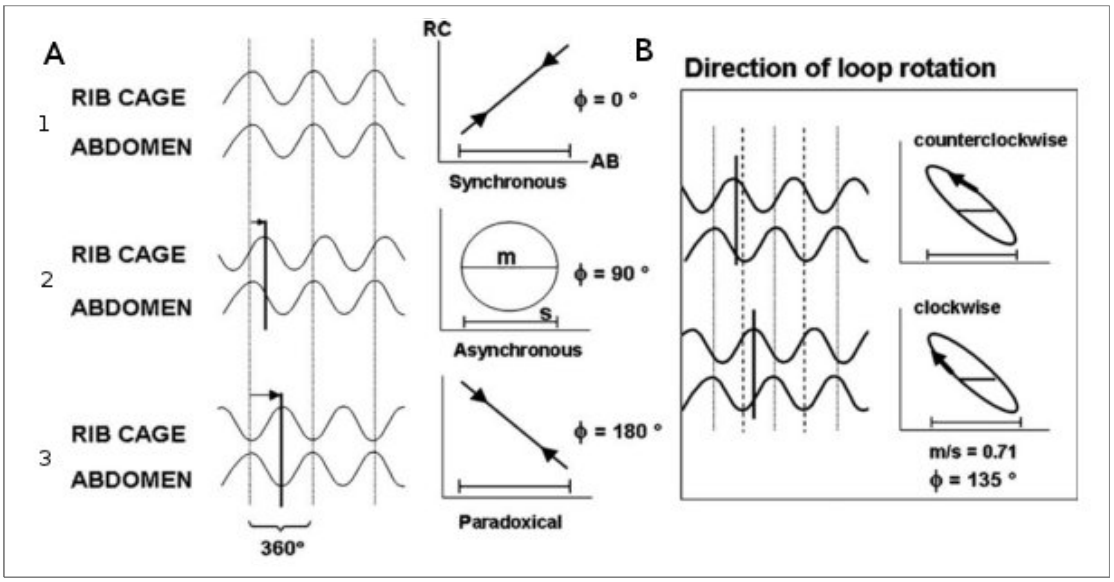


Figure 1.27 - Phase Angles 1 and Loop rotation 2 of the Lissajous figures indicates whether the diaphragm contracts before the intercostal muscles (anticlockwise) or the intercostal activity precedes the diaphragm (clockwise)

When RC and ABD move in perfect synchrony the phase angle is zero (Fig. 1.27 A1) .

As asynchrony appears the loop opens (Fig. 1.27 A2) .

Complete asynchrony (paradoxical movements) results in a phase angle of 180° (Fig. 1.27 A3).

Important information can also be obtained from the direction of loop rotation on the Lissajoux figures (Fig. 1.27 B).

Direction of loop rotations depends on which compartment (RC or ABD) precedes the other (Fig. 27 B). Anticlockwise loops plot indicate that the AB compartment (diaphragm) leads the RC as usually observed in normal quiet breathing. Clockwise loops instead signify the opposite.

The use of respiratory inductance plethysmography in combination with the phase angle analysis on the Lissajous figures can be finally, an helpful and intuitive approach to monitor and detect chest-wall asynchrony in COPD patients during mechanical ventilation.

This approach is part of the concept of the "new system of monitoring" and its implementation will be discussed and better explained in Chapter 3.

1.4.1.4 Monitoring and management in patient affected by COPD and Sleep disordered breathing

COPD is usually a progressive disease and not fully reversible [41].

Lung function can be expected to worsen over time, even with the best available care.

Symptoms and objective measures of airflow limitation should be monitored to determine when to modify therapy and to identify any complications that may develop.

An effective COPD management plan includes four components [41]:

- Assess and Monitor Disease;
- Reduce Risk Factors;
- Manage Stable COPD;
- Manage Exacerbations.

The goals of effective COPD management are to:

- Prevent disease progression
- Relieve symptoms
- Improve exercise tolerance
- Improve health status
- Prevent and treat complications
- Prevent and treat exacerbations
- Reduce mortality.

The follow-up of the patients' physical and mental condition is part of best practice, and this can be realized through the continuous monitoring patients' respiratory health status.

In subject affected by COPD and Sleep disordered breathing regular surveillance of patients' respiratory health status is recommended by GOLD [41] and also other guidelines [77] performing investigations on:

- **Pulmonary function:** a patient's decline in lung function is best tracked by periodic spirometry measurements although useful information about lung function decline is unlikely from spirometry measurements performed more than once a year. Spirometry should be performed if there is a substantial increase in symptoms or a complication. Other pulmonary function tests, and measurement of lung volumes are not needed in a routine assessment but can provide information about the overall impact of the disease
- **Arterial blood gas measurement:** screening patients by pulse oximetry and

assessing arterial blood gases in those with an oxygen saturation (SaO2) < 92% is a useful way of selecting patients for arterial blood gas measurement. Nocturnal oximetry is recommended to evaluate gas exchange during sleep in COPD patients to monitor nocturnal hypoxemia: it is also mandatory in order to titrate the oxygen flow adequately in patients who are candidates for long-term oxygen therapy (LTOT) [77].

- **Respiratory muscle function:** respiratory muscle function is usually measured by recording the maximum inspiratory and expiratory mouth pressures. More complex measurements are to research laboratories. Measurement of inspiratory muscle force is useful in assessing patients when dyspnoea or hypercapnia is not readily explained by lung function testing or when peripheral muscle weakness is suspected.
- **Sleep studies:** sleep studies are performed when there is a clinical suspicion of an associated sleep apnoea syndrome or manifestations of hypoxemia not explained by the presence of day-time hypoxemia or by the level of airflow obstruction.

Gathering information on some or whole of the recommended monitoring parameters, finally may serve to define the better management, fitted to subject and to the stage of severity.

1.4.2 Sleep Apnea-Hypopnea Syndromes: OSA e CSA

Sleep apnoaea-hypopnea syndromes are sleep disorders characterized by abnormal pauses in breathing or instances of abnormally low breathing, during sleep.

The term apnoea indicates a cessation of breathing during sleep, and it can occur together with hypopnoea that is a transient reduction in respiratory activity, brought out from a decrease of 50% from baseline in the amplitude of a valid measure of breathing during sleep [19].

Both apnoea and hypopnoea can be associated with oxygen desaturation consequential to the lack of adequate of alveolar ventilation that may bring to awakenings during night [18].

The standard definitions set the minimum duration of an apneic/hypopneic event on 10 seconds, with the con concomitance of either a sleep arousal, or a blood oxygen desaturation of 3-4% or greater, or both arousal and desaturation [19]

Generally, more than 5 of such events per hour are considered abnormal: diagnosis of a syndrome can is generally based on the demonstration of at least 5 apnoeas and hypopnoea

per hour of sleeps with the accompagnishment of one or more symptoms of snoring, restless sleep, morning headaches, and excessive daytime sleepiness. [18].

There are 2 major forms of sleep apnoea or hypopnoea: obstructive and central [25].

In obstructive apnoeas breathing is interrupted by a physical block to airflow despite effort resulting from complete or partial collapse the upper airways, whereas central apnoeas and arise from reductions in respiratory drive from the central nervous system.

If there were the prevalence of one of the forms in the general disease state, the syndrome can be classified as Obstructive Sleep Apnoea Syndrome (OSAS) or Central Sleep apnoea Syndrome (CSAS).

Obstructive sleep apnoea syndrome (OSAS) is the most common of such disorder, affects more man than women, and is strongly linked to obesity and cardiovascular diseases [20].

It is characterized by the repetitive collapse or partial collapse of the pharyngeal airway during sleep [16].

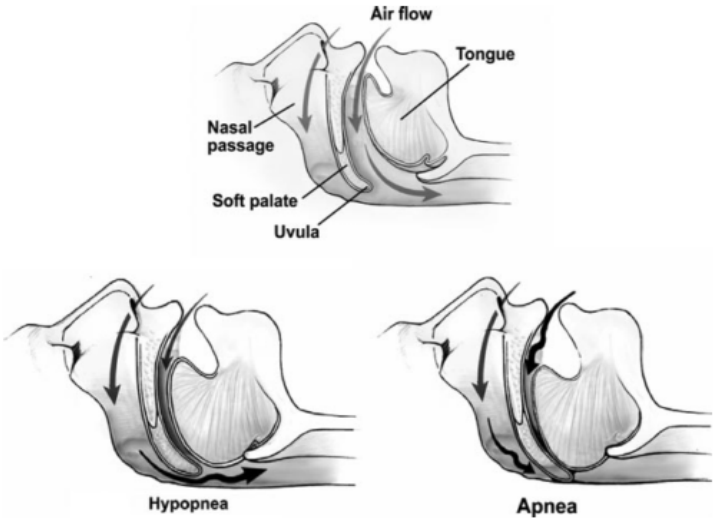


Figure 1.28 - Partial and complete airway obstruction resulting in hypopnoea and apnoea. Pharyngeal collapse in patients with OSA generally occurs posterior to the tongue.The primary abnormality in patients with OSA is an anatomically small pharyngeal airway resulting from obesity, bone and soft tissue structures, or, in children, tonsils and adenoids. The pathophysiology of obstructive apnoeas is complex and varies between patients.Although deficient pharyngeal anatomy and variable upper airway dilator muscle control awake and asleep are likely the predominant causes of pharyngeal collapse in most patients with OSA, other mechanisms also likely contribute Pharyngeal cross-sectional area decreases when functional residual capacity (FRC) is reduced, and oxygen saturation may also be volume-dependent: obstructive sleep apnoea tended to be longer when lung volume was increased [35].

During the subsequent apnoea or hypopnoea, hypoxia and hypercapnia stimulate ventilatory effort and ultimately arousal from sleep to terminate the apnoeic event.

Central sleep apnoea syndrome is characterized by repetitive cessation of ventilation during sleep resulting from loss of ventilatory drive [18]

The recurrent apnoeic episodes occur in the absence of upper airway obstruction during sleep with reduced or absent breathing and respiratory effort [19].

Central apnoeas during sleep may occur in a number of circumstances: decreased chemical drive or failing respiratory muscle function are associated with CSA, in particular in some sleep states.

The transition from wakefulness to sleep is an inherently unstable period in terms of cardiorespiratory control.

With sleep onset, there is a loss oft the wakefulness stimulus and behavioural influences: several respiratory control mechanisms are down regulate, ventilatory responses to hypoxia and hyper- capnia and respiratory load compensation are reduced across sleep stages, particularly during REM sleep [22].

The resultant reduction in ventilation is coupled in a gradually with a gradual rise in Paco2.

Thus, during sleep, chemoreceptor and respiratory reflex feedback become critical components.

Central apneoa is usually initiated during sleep by a further acute increase in ventilation and reduction in PaCO2, that may be triggered also by spontaneous arousal [27].

When PaCO2 Apnea persists until PaCO2 falls below the threshold level required to stimulate breathing, the central drive to respiratory muscles and airflow cease, and central apnoea ensues rises above the threshold required to stimulate ventilation [27].

Central respiratory drive can also be inhibited by upper airway reflexes [21].

Figure 1.29 schematically shows the arising mechanisms of central sleep apnoea

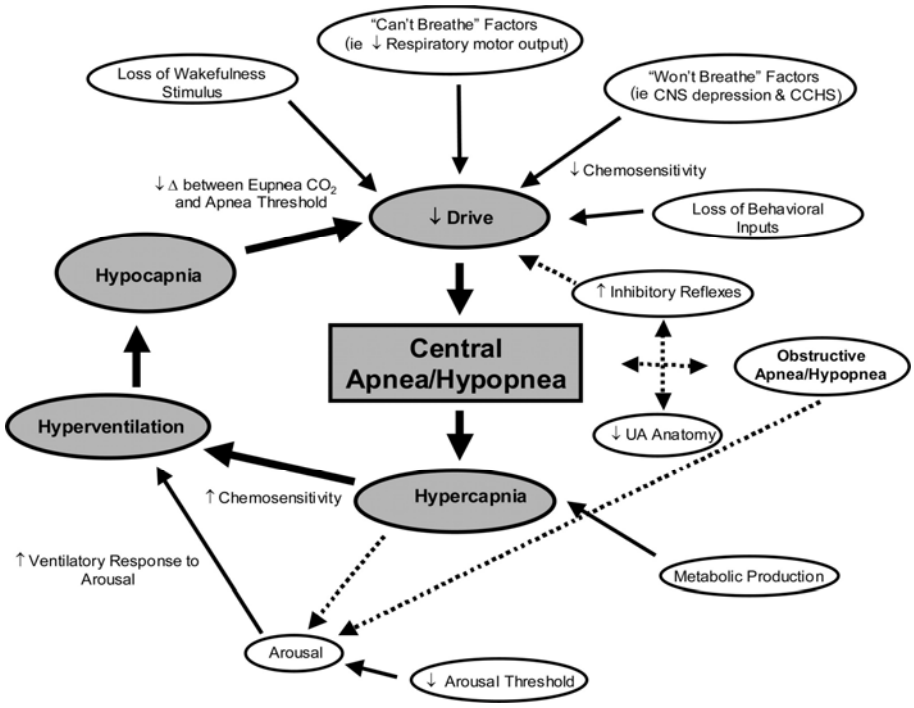


Figure 1.29 - Schematic of the many potential mechanisms contributing to CSA/hypopnoea

CSA syndromes can be broadly classified into two groups hypecapnic vs non hypercapnic. Hypercapnic central sleep apnoea overlaps with hypoventilation syndromes can be the result of metabolic or neuromuscular disorders [21], otherwise normocapnic or hypocapnic central sleep apnoea can arise with the weakening of chemoreceptor reflex due to cardiovascular diseases [19].

It has been proved that central apnoeas can be also a feature of Cheyne-Stokes breathing [37], which is commonly seen in patients with congestive heart failure: Cheyne-Stokes breathing a form of periodic breathing in which central apnoeas and hypopnoea alternate with periods of hyperventilation that have a waxing- waning pattern of tidal volume [27].

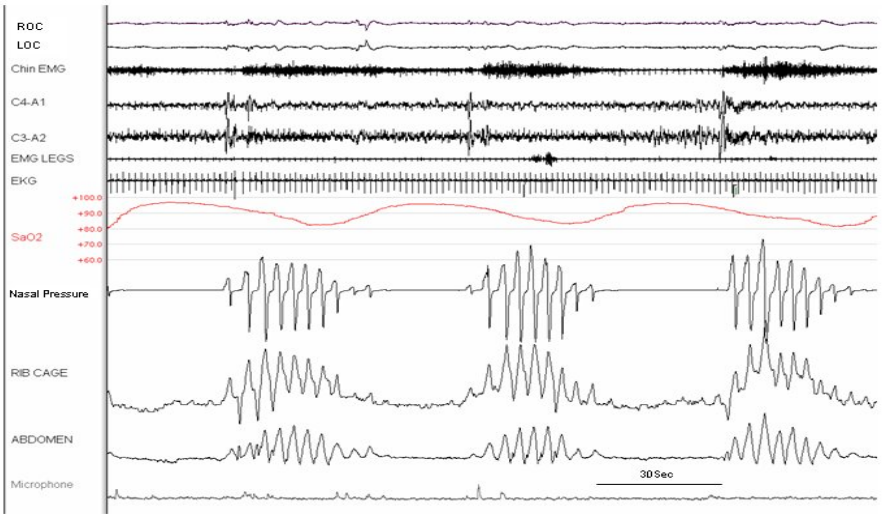


Figure 1.30 - Cheyne-Stokes breathing seen in a polysonnography recording

1.4.2.1 Effects of sleep apnoea on cardiovascular system

In healthy persons, physiologic sleep is associated with distinct sleep stage related changes in cardiovascular regulation.

Sympathetic nervous traffic to muscle, as well as heart rate, blood pressure, oxygen saturation progressively diminishes during deeper stages of non-REM sleep.

However, REM sleep is accompanied by striking increases in sympathetic drive.

Repetitive apnoeic events disrupt the normal physiologic interaction between sleep and cardiovascular system.

Intermittent apnoea induced hypoxia, hypercapnia, and arise to a progressive chemoreflex mediated increase in sympathetic activity with consequent vasoconstriction [28].

At termination of apnoea, sympathetic vasoconstriction is inhibited, the restoration of venous return and consequent is increased cardiac output, together with severely constricted peripheral circulation, results in acute increased in blood pressure[26].

These conditions predispose a patient acutely to cardiac ischemia and arrhythmias, and chronically could contribute to left ventricular hypertrophy myocardites, and ultimately, failure [25].

1.4.2.2 Intermittent hypoxia and oxidative stress related to sleep-apnoea

Intermittent hypoxia and reperfusion during repetitive episodes of nocturnal apnoea may be involved in the generation of highly reactive free oxygen radicals.

This phenomenon, which occurs frequently during each hour of sleep, every night, and over several decades in untreated patients, may elicit increased vascular oxidative stress.

Hypoxic stress induced by OSA oxidative stress may cause inflammatory responses in lung parenchyma [16]

An experimental study conducted by Farrè et al [38] tested that high-rate intermittent hypoxia with a time course similar to that found in OSA (one or more hypoxic event per minute) on mice enhances tumour growth.

Some efforts at this studies comes from Renke et al [83], that have shown how intermittent hypoxia increases lung volume and alveolar surface area and upregulates genes of lung growth in adult mice. This suggests that intermittent hypoxia could play an important role in regulating the various stages of tumour formation and progression in lung cancer.

1.4.2.3 Diagnosis and monitoring of Sleep Apnoeas

Polysomnography is the most rated and recommended test for the diagnosis and the monitoring of sleep apnoeas [19.35]. The test is an overnight study during which multiple physiologic signals are monitored in the sleeping patient.

The parameters measured are:

- Electrooculogram (EOG), to pick up the activity of the eyes.
- Elecrtoencephalogram (EEG), to monitor the brain activity.
- Electromyogram (EMG), to monitor the activation of respiratory muscles
- Electrocardiogram (ECG), to monitor heart activity.
- Oral and nasal airflow.
- Thoracic and abdominal movements.
- Blood oxymetry, to determine changes in blood oxygen levels.
- Sleeping position.
- Snoring.
- Legs movements.

The measurements of such information can lead to a primary diagnosis of sleep apnoeas, and further to an identification of the type.

In obstructive sleep apnoea they can show pauses in breathing. As in central apnoea, pauses are followed by a relative decrease in blood oxygen and an increase in the blood carbon dioxide.

Whereas in central sleep apnoea the body's motions of breathing stop, in obstructive sleep apnoea the chest not only continues to make the movements of inhalation, the movements typically become even more pronounced: CSAS should be distinguished from OSAS by demonstrating that there is reduced or absent respiratory effort in the former and maintained or increased respiratory effort in the latter

Additionally, arousals that typically terminate an obstructed breathing event, occurs in CSB, in association with the peak of ventilation in any cycle of breathing[19].Current standards recommend using non-invasive methods capable of discriminating between obstructive and central events, such as respiratory inductance plethysmography [34]

Though the polysomnography test can be also measured the number of apneic/hypopneic event occurred, in order to evaluate the severity of the syndrome.

The number of apnoeas and hypopnoea per hour of sleep, also called apnea-hypopnea index AHI is the index most commonly used to determine the severity of OSA. with no validated standards regarding severity classification.

The current clinical practice has adopted the following classification of severity [19]:

Mild: 5 to 15 events per hour

Moderate: 15 to 30 events per hour

Severe: greater than 30 events per hour

The usefulness of the polysomnography recording stays in its capability to monitor sleep structure, cardiac rhythm, oxyhemoglobin saturation, and respiration: this can provide a complete vision of the pathological state and of the potential comorbities.

1.4.3 Sleep in COPD and sleep breathing disorders

Sleep has effects on breathing. In healthy subjects during sleep, respiration presents a general depression. Ventilation, breath frequency and inspiratory decrease [13] and the net effect of these changes is relative alveolar hypoventilation, which is particularly pronounced in rapid-eye-movement sleep.

Thus gas, exchange is altered [77], with a small but significant reduction in PaO2 and an

increase in PaCO2. Also chemoreceptor sensitivity and respiratory control show variations. The normal ventilatory responses to hypercapnia and hypoxia that occur during wakefulness are blunted in sleep: the ventilatory and arousal responses to hypercapnia are much more robust than those to hypoxia, making the decrease in PaCO2 is a potent arousal stimulus

Sleep is, therefore, a physiological state that produces an increased breathing load [77]

Respiratory muscle activity and chest wall motion varies differ markedly in the various stages of sleep otherwise and airflow resistance increases [77].

The changes in the activity of the respiratory muscles are associated with a marked reduction in the rib cage's contribution to tidal volume and, consequently, a greater reliance on the diaphragm to maintain ventilation.

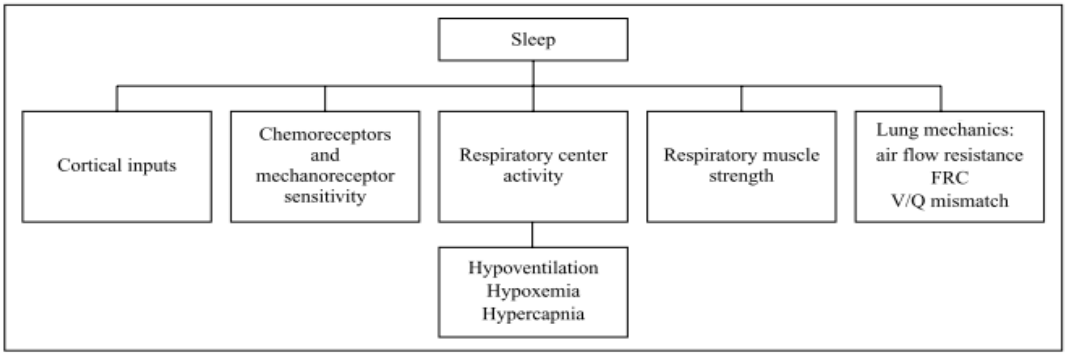


Figure 1.31 -The principal factors that operate in controlling breathing during sleep (FRC: functional residual capacity)

The sleep-related modifications in the respiratory system do not induce adverse effects in healthy subjects, but may cause problems in patients with chronic obstructive pulmonary disease [78].

Hypoventilation, worsen by diaphragm weakening and concurrent physiological increased breathing load (cfr 1.4.2.2), causes the most important gas-exchange alteration during sleep in COPD patients, leading to hypercapnia and hypoxemia, especially during rapid-eye-movement (REM) sleep.

Nocturnal hypoxemia and the consequent oxygen desaturation is the most significant sleep abnormality associated with COPD.

Even without any upper-airway contribution, various studies have reported that 27–70% of

patients with COPD with awake oxygen saturation of 90–95% can experience substantial desaturation at night, particularly during REM sleep [76].

Nocturnal oxygen desaturation can be defined or measured in terms of oxygen nadir, the lowest saturation recorded during the study, or time below some oxygen-saturation limit, such as 88% or 90% [75]

Arousals may be related to episodes of desaturation, these consequences might help explain why nocturnal oxygen desaturation is a marker of increased mortality, and why COPD patients are reported to die more frequently at night than expected.

Blood gases alterations lead to increased arousals, sleep disruption, pulmonary hypertension and higher mortality.

The presence of other sleep-related breathing disorders, like sleep apnoea syndrome, may induce a more pronounced impairment of gas exchange, both during sleep and wakefulness, and development of symptoms like excessive daytime somnolence.

1.4.4 Mechanical Ventilation for chronic respiratory disease treatment

Mechanical ventilation is a method to mechanically assist or replace breathing in patients with impaired respiratory system.

Mechanical ventilation is defined as the provision of the minute volume of respiration by external forces.

It is usually required when there is impaired action of the patient's respiratory muscles, a severe dysfunction of the mechanics of breathing or a limited respiratory drive.

During quiet breathing the pressure applied to the respiratory system is the pressure developed by the respiratory muscles (Pmus). While, in a ventilated patient, Prs is equal to the sum of the pressure generated by the ventilator (PVE) and Pmus.

Thus when the patient's breathing activity is entirely passive (full ventilatory control), pressure developed by the respiratory system muscles is negligible, and the driving pressure is fully delivered by the external forces (Figure 1.32).

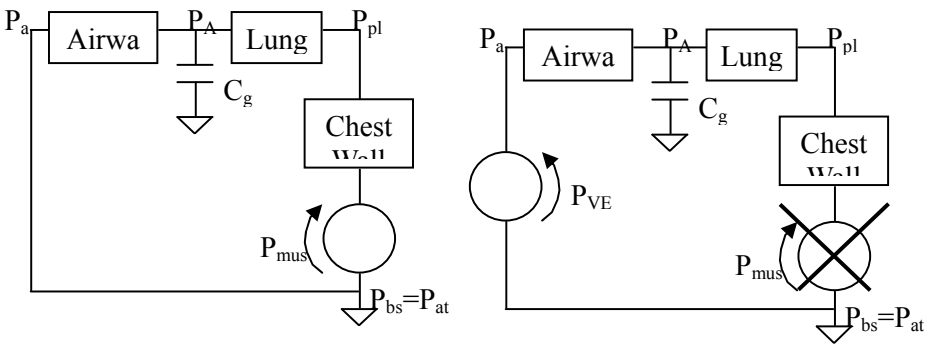


Figure 1.32 - Respiratory system model during: left) quiet breathing; right) fully ventilator control

The device which generates the external forces to assure the right volume of air to deliver is called *mechanical ventilator* (Figure 1.33).

Figure 1.33 - Mechanical Ventilator

Figure 1.34 shows the functional schema of a mechanical ventilator:

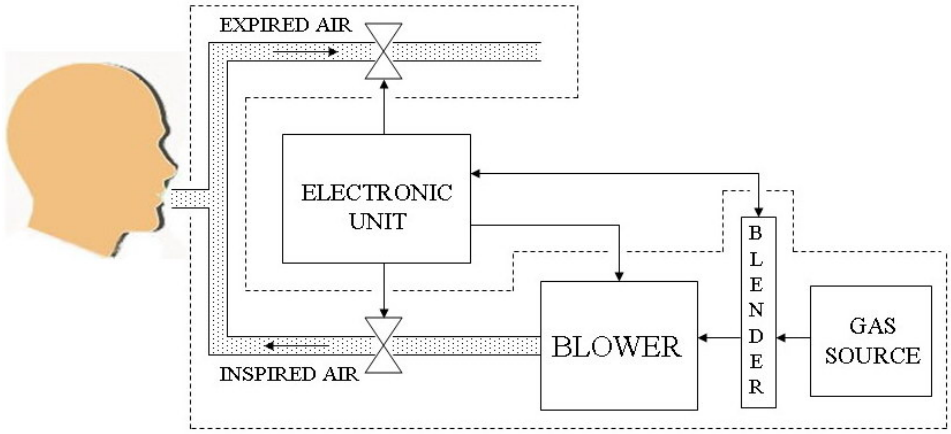


Figure 1.34- Functional Scheme of a Mechanical Ventilator

It consists of 2 main blocks:

- *Pneumatic unit*: it includes all the mechanical components that physically control gas delivery and that are directly connected with the patient. The pneumatic system includes also a *gas source*, and a *blender* to establish specific oxygen concentrations. Both the systems provide gas concentrations to the *blower*, that modifies the air flow
- *Electronic unit:* it includes the devices required to perform all the logical operations to assess the selected ventilation mode properly, to impose the control variable in dependence of the selected ventilation mode, and to handle the alarm systems.

There are two major ventilation modalities that concern the connection between patient and the ventilator: invasive and non-invasive ventilation.

The first modality is used for more severe cases and air is delivered with an endotracheal tube connected directly to the patient's airways.

Non-invasive ventilation (NIV) is commonly used in less critical situation and during the weaning period: in NIV air is delivered through nasal or oronasal mask like the one shown in Figure 1.35.

Figure 1.35 - Oronasal Mask

Non-invasive Positive Pressure ventilation (NPPV) refers to non-invasive ventilation that

provides air at positive pressure that is greater than the atmospherical one.

Distinguished by the temporal deliver of the positive pressure there are several modalities of NPPV. For the treatment of COPD and OSAS the two most common are:

- *CPAP in which a positive constant pressure* flow is delivered: the pressure is higher than the atmospheric pressure and equal to the pressure at mouth at the end of espiration (*PEEP Positive End Expiration Pressure)*. This is the most common modality used for OSAS treatments.
- *VPAP, or variable positive airway pressure*, also known as bi-level or BiPAP, that provides two levels of pressure, one for expiration (EPAP Expiratory Positive Airway Pressure, equal to PEEP) and one for inspiration (IPAP Inspiratory Positive Airway Pressure). If the patient breaths spontaneously the ventilator synchronizes with the respiratory rhythm. This modality needs more expensive ventilators, and is sometimes used with patients who have other coexisting respiratory problems and/or who find breathing out against an increased pressure to be uncomfortable or disruptive to their sleep.

Non-invasive positive-pressure ventilation is a primary treatment for patients with exacerbations of chronic obstructive pulmonary disease [79].

It is preferentially indicated during sleep periods, in order to achieve longer duration of ventilation; this is probably necessary to compensate nocturnal hypoventilation and episodes of arterial oxygen desaturation which occur predominantly during rapid eye movement sleep when breathing room air [119].

Indeed, the main beneficial effect of NPPV implies a correction of nocturnal hypoventilation and PaO2 reduction is the hallmark of improvement in alveolar ventilation under all types of mechanical ventilation. Such an improvement could persist after interruption of the ventilation period because of a temporary improvement in CO2 sensitivity of the respiratory centres.

The improvement of nocturnal PaO2 could also lead to an improvement of the diurnal PaO2 [80], an effect that can be related to the correction of the alveolar-arterial gradient under NPPV and to the increase in spontaneous breathing pattern following mechanical ventilation. Non invasive ventilation can be also applied in patients that require long-term ventilation assistance at home, using special designed home-ventilators previously set by respiratory therapists and/or physicians.

Chapter 2 - Home respiratory Care

2.1 Telemedicine, e-Health and Home telehealth

Since the 90's information and communications technologies (ICT) are used in the practice of medicine and one of the oldest and most known terms about the employment of ICT in healthcare is “telemedicine”.

Telemedicine has been defined as the “*use of advanced telecommunication technologies to exchange health information and provide health care services across geographic, time, social, and cultural barriers*” [Choi et Al. 92].

The concept of telemedicine is not new.

Beyond the use of the telephone, there were numerous attempts to develop telemedicine programs since the 1960s.

However, due to the shift in the telecommunications industry from analog (voice-oriented) to digital (data-oriented), and with the advent of cellular phones and other mobile telecommunications technologies, such as the GSM , GPRS UMTS 3G and the emerging 4G, telemedicine today is much more sophisticated than what it used to be.

A few years ago, the term eHealth aroused, defined by Eysenbach as “*eHealth is an emerging field in the intersection of medical informatics, public health and business, referring to health services and information delivered or enhanced through the Internet and related technologies. In a broader sense, the term characterises not only a technical development, but also a state-of-mind, a way of thinking, an attitude, and a commit- ment for networked, global thinking, to improve healthcare locally, regionally and worldwide by using information and communication technology*” [101].

Telemedicine or e-Health usually comprises a number of facilities.

Examples include health information networks, electronic health records, telemedicine services, wearable and portable systems which communicate, health portals, and many other ICT-based tools assisting disease prevention, diagnosis, treatment.

Application of telemedicine and/or telehealth to the home environment is usually described as **home telehealth** or **home based eHealth** [102]**.**

Practically home telehealth consists in the application of data gathering, communication,

storage, and manipulation technologies and techniques to health care delivery in the patient's home: more widely than telemedicine does, it encompasses preventative, promotive and curative aspects [102].

In home-telehealth usually two participants are involved, the caregivers and patients. Four common uses of telemedicine are identified:

- *Teleassistance*: physician assists a patient who is geographically isolated.
- *Telemonitoring*: transmission of medical information for monitoring purposes.
- *Teleconsultation* (patient-caregiver): patients seeking for medical advice.
- *Teleconsultation* (caregiver-caregiver): one caregiver helps the other one.

In general, home telehealth adds a new paradigm that can be useful to face the challenges that currently health care systems all around the world have to face.

In the current context of economic pressures and a desire to secure efficiency savings, there is significant interest in the potential for technology to reduce utilisation of health services in older people with long-term conditions and social care needs, while improving the quality and cost-effectiveness of care [104].

Even if the opinion in matter is controversial several studies shows how the application of home-telehealth can be cost saving and can reduce the number of hospitalizations [99-104].

As telemedicine is widely considered to be part of the inevitable future of the modern practice of medicine, it is crucial that any barriers to the effective use of telemedicine be identified and remedied without delay. Specifically, there are a number of unresolved standardization issues that need to be addressed before telemedicine may be used in the most efficient and effective possible way [92].

Because of their long term nature and to their epidemiology that affects mostly older people, chronic diseases such as COPD and OSAS are particularly suitable to be managed by home -telehealth.

Home-based programs offering nursing care or pulmonary rehabilitation provide possible alternatives to hospital admission with lower costs mostly for the patients those are in exacerbation [103].

2.2. Telemonitoring

Telemonitoring can be considered an implementation of home telehealth.

It involves the use of telecommunication technologies for the transmission of biometrical data such as spirometric measures, biological signals, or other information like symptoms, and medications use in order to monitor patients conditions at a distance [95].

It has been defined by the American Telemedicine Association, as the remote *monitoring that occurs between the health care provider and patients in their place of residence. Patient outcome data are transmitted to a health care provider from a remote location* [97].

Home telemonitoring services can be classified as *synchronous* (real-time interaction) or *asynchronous* (not real-time).

Synchronous technologies refer to information and communication technologies that enable individuals to communicate live over long and short distances.

Such technologies include live measurements, audio and video conferencing.

Asynchronous telemonitoring instead involves the storage of clinical digital samples and relevant data, which are forwarded to a health care professional at a distant site, by email or through the Internet, as video clips or other forms of data transmission, for assessment at a convenient time.

The classical home-based telemonitoring service architecture is composed by three entities *(Figure 2.1)*.

- *home site*: consists of software, hardware, and services that are used to assist in managing and monitoring the client's condition. In the home site, the requested data on patient's health are acquired by a medical device linked to the network through a *network interface*. The acquisition can be fully automatic or performed through the patient's action, according to guidelines provided by a physician.
- *Communication network*: Hardware, software, network, and communication infrastructure required for data delivery. The network infrastructure can allow monodirectional (*half-duplex*) or bidirection (*full-duplex*) communication and should guarantee the reliability of the connection in order to prevent data loss during the transmission. Typical network infrastructure are based on Ethernet or mobile services such as GSM, GPRS, UMTS satellite or the the newest 3G, 4G

technologies.

- *healthcare site:* software and hardware used to assist clinicians in managing multiple patients, collecting displaying and storing the transmitted patients' data. It includes also clinical staffing and the professional services that are necessary for consultative support to users and clients using home telemonitoring.

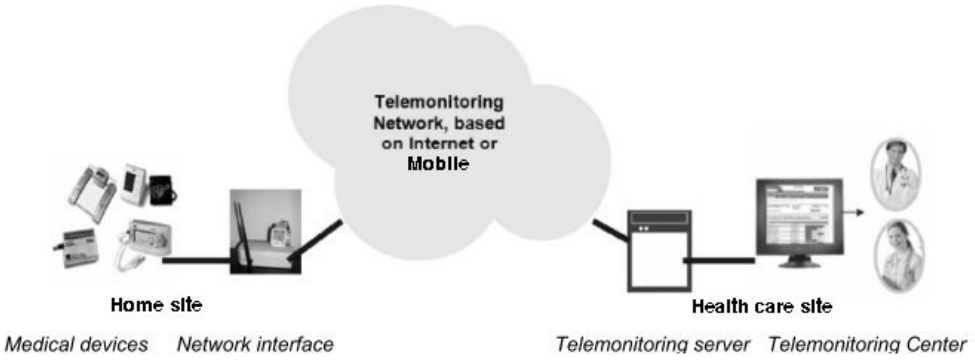


Figure 2.1 - General Architecture of a telemonitoring system

The effectiveness of the telemonitoring in clinical practice is still controversial [99,100], but it is certain that it adds new capabilities to healthcare services such as:

- *removal of physical distance*, allowing clinical support to be provided to the patient without clinician and patient being in the same physical location.
- *provision of time series data* enabling the development of a condition to be monitored against parameters and algorithms that check for problems more frequently and to positively trigger alerts when additional support is needed.
- *engagement of the patient directly in measuring the objective signs* related to their own condition as well as the subjective symptoms providing a permanent comprehensive record of readings and feelings that can be reviewed and discussed with clinicians

2.3 Telemonitoring for chronic respiratory diseases

The increasing demand for health services due to the ageing of the population has recently led to a growing interest in e-health and telemedicine applications for the management of chronic diseases [111].

This trend is evident and valid also for chronic respiratory disease such as COPD and sleep disordered breathing like OSA, whose prevalence is expected to increase in the future.

Chronic respiratory diseases represent a wide category of chronic illnesses that have significant effects and burdens on society: these medical conditions necessitate education, self-monitoring, and close management to ensure better outcomes and to prevent exacerbations, complications, and potential death.

Chronic respiratory diseases have become major causes of death in almost all countries.

Such prevalence of chronic diseases is one reason why expenditures on health care are skewed: in most health care delivery systems, 5% of patients can be responsible for 50% of costs [115]. Untreated patients with OSAS have an estimated annual medical cost of $2,720 per patient versus $1,384 for age and gender matched controls.

Comparable numbers were calculated for patients in Canada and Europe [117].

However, diagnosis and treatment of sleep-disordered breathing produce high incremental charges to the health system as well.

Although they range widely, charges cited for an attended polysomnogram (PSG) in the sleep laboratory with interpretation are about $1,200 per patient per night [116].

The management of chronic respiratory diseases and sleep-related respiratory disorders is thus, an area of great potential for telemedicine and home care because of the high prevalence and chronic nature of these disorders.

Possible applications include both the sleep-related respiratory disorders in the strict sense of the term (obstructive sleep apnoea- hypopnoea syndrome and Cheyne-Stokes respiration) and also the diseases which, without being specific to sleep, are nonetheless associated with nocturnal respiratory abnormalities or give rise to the need for ventilatory support during sleep [100].

Several studies reported the use of telemonitoring systems and technologies that assist in quality control of measurements taken at home and in identification of incorrectly performed pulmonary function tests.

In literature the application proposed are different: some studies have been carried out on

the telemetric transmission of physiological parameters while the patient is sleeping [122, 123] and on home mechanical ventilation [124.125].

Other uses for telemedicine that have been proposed are the monitoring of treatment with continuous positive airway pressure (CPAP) with a view to improving effectiveness and patient compliance [126,127]

Like the most of telemedicine applications in the field of respiratory medicine, the studies performed have been exploratory and the findings have not yet been confirmed.

An extensive literature review conducted by Bartoli et al. [103] identifies the relevant telemedicine applications in respiratory care and in particular in COPD treatment.The research analysis had led to recognise *telemonitoring* as the most common service among the organizational models of telemedicine and in general, most telemonitoring studies presented positive results in relation to acceptance of the systems and telemonitoring programs.

The most important clinical implication of home telemonitoring relates to the ability of healthcare professionals to contact patients in a timely manner and to perform necessary changes in their home management plans and therapies based on data received from patients before complications or exacerbations take place.

Furthermore increased feelings of security and reassurance and control over their medical condition, better knowledge and awareness about their disease, contribute to an improvement of disease condition.

However, the use of complicated procedures for data transfer was associated with poor compliance, as opposed to applications with reminders and prompts, which were associated with good patient adherence.

Overall, ease of use and friendliness of the technology and monitoring equipment may have contributed to good compliance among patients and their acceptance of the telemonitoring system.

The technology used plays an important role not only for the patient acceptance, but also in the economic sustainability of the telemonitoring infrastructure.

Even if it is true that such technologies should be very reliable, their application often requires the patient's home to be equipped with a computer and an Internet connection, often of high specifications and bandwidth[110].

These requirements have been an obstacle to the use of telemedicine among elderly

patients and patients with a low socioeconomic level [110].

A centralized ICT model may perhaps be appropriate for the operation of an established medical application, but the use of a centralized model in applications that are still under development, often leads to failure.

It is, in fact, almost impossible to study the cost-effectiveness of telemedicine because the technology cannot be applied without a complex and expensive ICT platform.

On the other hand, the ICT companies and hospitals do not develop these platforms because of the lack of studies supporting their cost-effectiveness.

As a result of this series of consequences, respiratory telemedicine is a much less developed and established application than might be expected in view of the advanced technological solutions now available.

An interesting new direction is indicated by the development and commercial availability of telecommunications technology that makes it possible to decentralize the communications architecture used for telemedicine, particularly in the domain of sleep disorders.

Using the low-cost miniature integrated circuits now available on the market, devices can be created that are able to do all of the following tasks:

- capture the digital signals produced by any conventional device (such as a CPAP device, a home ventilator, or a pulse oximeter);
- send control signals to any device (for example a control signal that modifies the parameters of a ventilator)
- function as an Internet server by way of a conventional mobile telephony SIM card with its own web address and password.
- send data in real time

These 4 characteristics represent the most significant change in the model.

Immediate and inexpensive 2-way communication can be established by connecting such a device to the CPAP device or ventilator, thereby enabling continuous monitoring of the patient and control of the ventilation parameters from any location with Internet access.

Moreover, this point-to-point connection between the patient and the medical professional monitoring the home treatment does not require a complex platform specifically designed to facilitate telemedicine, and the patient's home does not have to be equipped with any telecommunications infrastructure (computer or Internet connection).

It is reasonable to expect that the implementation of recent and future advances in the development and commercialization of telecommunication technologies will facilitate the more widespread application of telemedicine, both in terms of studies undertaken to evaluate the cost-effectiveness of telemedicine applications and the eventual incorporation of these technologies into routine practice.

In the next paragraph, the *Home Mechanical Ventilation Monitoring System* developed by TBM Lab is presented: this system implements the new ways of telemedicine approach already discussed, allowing a constant monitoring of pressure and flow of patient ventilation through a remote cheap and simple device connects via a GPRS network to the internet.

2.4 Home Mechanical Ventilation and Monitoring System(HMVMS)

Home Mechanical Ventilation (HMV) is provided by the hospital where health professionals furnish and titrate the ventilator during a short setting up session which, in many cases, does not include a sleep trial.

Furthermore, after few days after the hospitalization, the titration parameters become no more optimal fitted, due to the changes in environmental and clinical conditions, to influences of every-day life, and also to the modification of ventilation required during the treatment itself.

Remote titration at home however could be realized by the continuous monitoring of the parameters of exchanged flows and volumes between patient and ventilator, and other physiological parameters.

At the actual state of the art, monitoring the patient and modifying the ventilator settings at distance is difficult in practice because it requires bidirectional telemetric data transfer: ventilation signals from patient's home to the HMV provider and ventilator control signals from the HMV provider to the patient's home [120].

Such a bidirectional tele-monitoring and tele-control system has been realized and proposed by TBM-lab and it is described in the next paragraph.

2.4.1 Home Mechanical Ventilation Monitoring System

In the management of chronic respiratory diseases with NPPV, the setting of correct ventilation parameters is essential for the success of ventilation strategy.

Nowadays it was not possible to assess breath-by-breath the optimal PEEP level to a given patient non-invasively and in clinical practice, especially during non-invasive ventilation.

Nevertheless it is important that ventilator parameters could be adjusted depending on the necessities or the situation, which could vary significantly in time.

At the actual state of art there are some automatic methods for titrating nasal pressure in SAHS patients is based on the use of automatic CPAP devices during sleep in the patient's home [121]. These devices measure various respiratory variables in order to detect breathing abnormalities (apnoeas, hypopnoea, flow limitation and snoring) by means of built-in pressure and flow sensors; the machine then uses proprietary algorithms to modify nasal pressure automatically and normalize breathing.

Unfortunately, automatic CPAP titration at home is not applicable to a non-negligible number of SAHS patients for instance, in patients with significant co-morbidities [121]. Furthermore, it could also be possible that the automatic unattended procedure fails in some eligible patients because of a lack of feedback or psychological support from sleep lab staff.

The *Home Mechanical Ventilation Monitoring System* (HMVMS) developed by TBM Lab of the Department of Bioengineering of Politecnico di Milano permits a constant real-time monitoring of pressure and flow of a patient ventilation allowing physician to tailor the ventilator and choose the best values for the single patient, every time he connects to the remote device.

The system is based on a simple and low cost data transfer server (DTS) (Figure 2.2) that acts as a web server requesting authentication information using a conventional GPRS mobile data network.

As an independent point-to-point communication is ensured and achievable by this approach, a hospital service or a private practice physician can receive real-time or previously recorded data and modify the settings of the ventilator by simply connecting, via Internet, to the individual web address of the DTS at the patient's home.

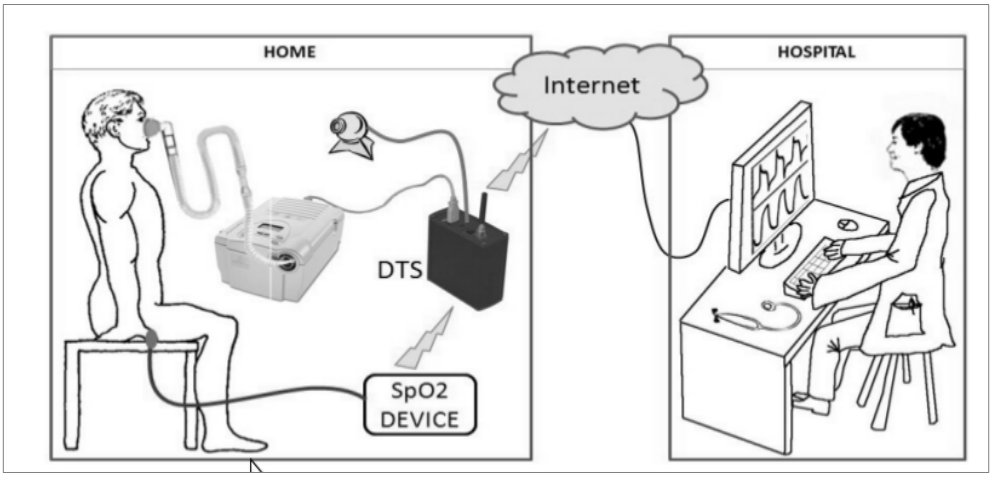


Figure 2.2 - Architectural scheme of the whole system. On the left is shown the patient at home, that can be seated or lying. On the right is shown a physician at the hospital who is watching at the real-time data on his computer. The DTS and the computer are both connected to Internet.

The DTS can be connected to most commercially available CPAP and BiPAP ventilators: the whole system comprises also an infrared webcam, and a SpO2 device that samples data from the patient.

The DTS is capable of sending different signals from the ventilator (patient's flow, pressure, tidal volume, mask leaks, oxygen saturation and heart rate) and patient's snapshots to the physician, through the infrared webcam, that is also suitable for night vision.

It allows the physician to directly control and change the ventilator settings, both titrating the ventilator for patients that require a more complete respiratory parameters analysis, and verifying that the ventilation settings are the best one for the actual conditions of the patient.

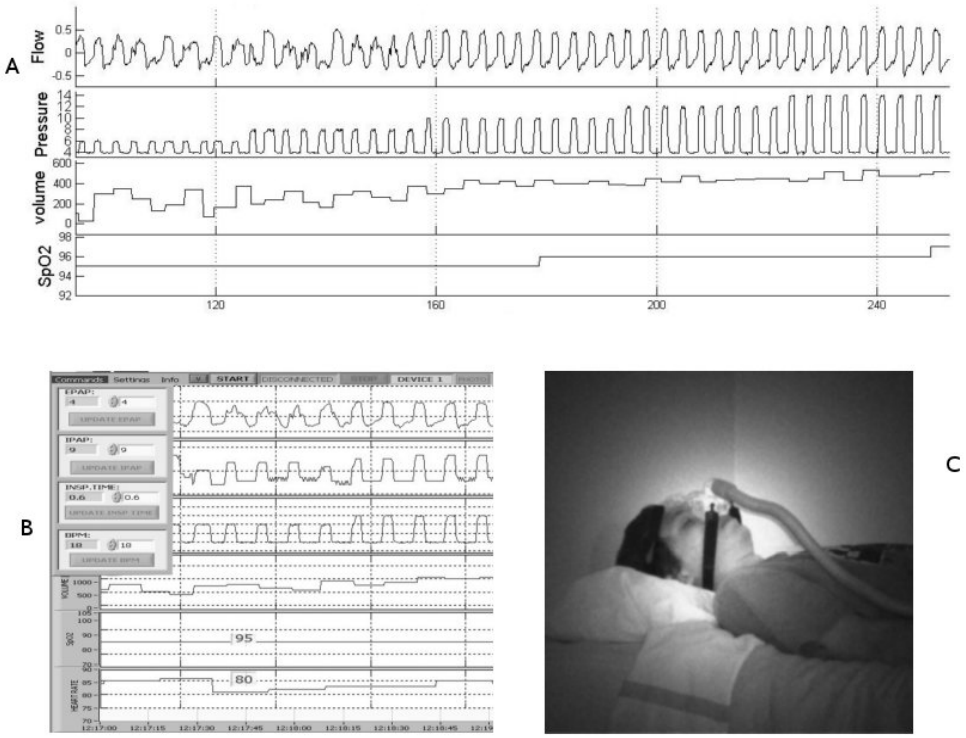


Figure 2.3- DTS Acquisition

A. *Traces of his graph the traces of Flow, Pressure, Volume and SpO2 acquired during a functioning test are shown.* ***B****. Zoom on a screenshot of the software installed on the physician computer that allows to see the traces and to control the ventilator through the menu showed it is possible to see in the upper right corner the button (PHOTO) used to send the request for a screenshot.* ***C.*** *Example of a picture of a sleeping subject taken with the infrared camera and transmitted though the described system.*

2.4.3 The novelty of HMVMS and a proposed improvement

The concept brought up by the HMVS, where a telemetry unit is connected to a commercially available ventilators, permits a low-cost (1.5€ per night per ventilator) [121], two-way communication channel in real time between the sleep lab technician and the ventilator in the patient's home.

This represents a novelty respect the traditional telemedicine approaches to chronic respiratory disease home care, which are nowadays limited to support the patient in order to improve treatment compliance or to remotely download previously recorded data[121].

The system does not require special telemedicine platform in the patient's home nor his/her active cooperation: it is therefore applicable to homes from a wide range of socio-economic levels.

A pilot study on the use of HMVMS showed the feasibility and effectiveness of such an approach for the remote titration of CPAP devices for OSA patients.

This study shows how it is possible to carry out a titration by a sleep technician instead of by an algorithm operating in the automatic CPAP machine [121].

Even if the HMVSMS can represent a great improvement in telehealth approach of chronic diseases management, providing the possibility of real-time, personalized and responsive home ventilation treatment, there is still one aspect that the system as has been described do not cover in a patient focused prospective.

At the actual state of development of the system, the evaluation of patient status that leads to titration control, is realized indirectly by the parameters got from the ventilator and directly only by the information from the Webcam snapshot and pulsoxymeter SpO2 signal.

This offers only a partial vision of the matching between the patient and the ventilator, and this vision is unbalanced on the ventilator side.

No data on the chest wall mechanics are gathered and only the SpO2 signal can be considered as an indicator of the cardiovascular response of the treatment.

This not totally complete assessment of patient's condition doesn't permit the identification of important abnormal respiratory events elicited by the affection from common chronic respiratory diseases. Some examples are chest-wall asynchronies in COPD or interruption of breathing in central sleep apnoea described in Chapter 1.

Allow the monitoring of such and other events directly from the patient's biosignals, can be

an important improvement on the current system: it furnishes indeed to the physician, more indication for the correct ventilator titration and finally provide a better disease management.

The implementation of this improvement, proposed in this thesis work consists in the integration of wearable sensor T-shirt to the home mechanical ventilation monitoring system.

The wearable system has been developed and tested in a European telemedicine project for chronic respiratory disease monitoring called *CHRONIOUS*.

The sensorized T-shirt can record several signals from the body like electrocardiogram, skin temperature, and blood oxygenation and heart rate.

It permits also the performance of a real-time respiratory inductive plethysmography through two inductive bands which measure respectively thorax and abdomen volume displacements.

Finally, it can gather information from the surrounding environment through two sensors that capture external temperature and humidity, and patient's skin temperature.

In the next chapter the Chronious project framework and the wearable sensored T-shirt will be better and more technically described as well as the solution implemented to integrate the wearable T-shirt in the whole home mechanical ventilation monitoring system.

Chapter 3 - Materials and Methods

3.1 The integration of the wearable system in the HMVMS

Patient adaptation is an important issue for the success of a respiratory care therapy that involves mechanical ventilation.

Air should be provided by the ventilator with the correct values of volume and pressure, in order to supply to the respiratory abnormalities due to the disease state.

A good and synchronized matching between patient breath variations and air delivering is a key factor for the efficacy and the responsiveness of the treatment.

Air delivering control should be realized under a constant monitoring of patient's state: this can be guaranteed in hospital where the monitoring equipments are normally disposable, but it not so easy in home care applications.

As exposed in Chapter 2, the Home Mechanical Ventilation Monitoring System by TBMLab of Politecnico di Milano permits a remote real time titration of the ventilator.

The titration is done by a technician, on the basis of the signal sent by the DTS system that gathers and transmits parameters from the ventilator, snapshot from the Webcam and finger SpO2 signal from the pulseoxymeter.

In order to realize a better patient's state monitoring, this thesis work proposes to integrate a wearable sensored t-shirt to the HMVMS.

The wearable sensored t-shirt was originally a part of the equipment of a telemonitoring project called Chronious.

CHRONIOUS, is a FP7 European project, which addresses an open integrated platform, based on multi-parametric sensor data processing for the long-term monitoring [131] of people suffering from chronic diseases.

The Chronious project aims to create a platform that evolves in monitoring patient's health status in a highly personalized level: it suggests the implementation of generic system architecture to be easily adapted to any chronic disease management program.

One of the main modules of the Chronius framework is the wearable system.

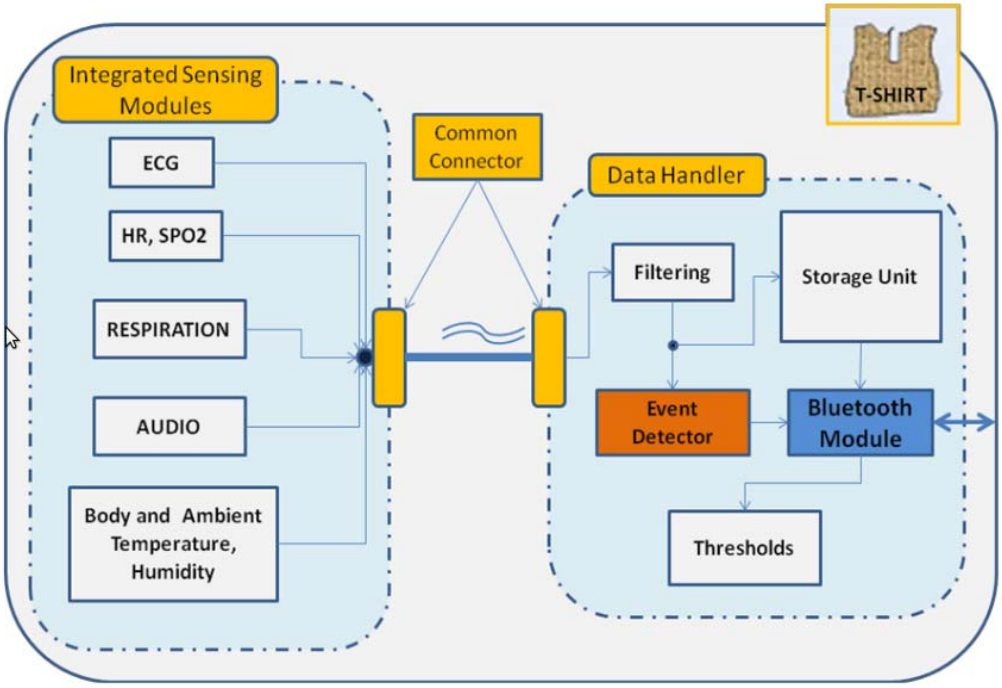


Figure 3.1 - Chronius Wearable System

The wearable system is composed of a shirt made of washable stretch-material into which integrates several sensors gathering vital signals directly from the patient's body.

It can perform a 3 leads electrocardiogram, a two bands real time respiratory inductive plethysmography, and finally it can measure skin temperature, blood oxygenation and heart rate.

It can also capture environmental information of external temperature and humidity and audio signals from the surroundings.

The data coming from the sensors can be sent via a wireless Bluetooth communication through the Data Handler, a microcontroller-based acquisition system connected to the t-shirt.

As shown in Figure 3.1 the basic idea underlying the integration of the wearable sensored t-shirt in the whole system, is to wireless connect it to the DTS through the Bluetooth technology, using an USB Bluetooth dongle connected to the DTS.

Bluetooth indeed, offers a non-dangerous wireless mode to transmit data and can be safely use for medical applications [131].

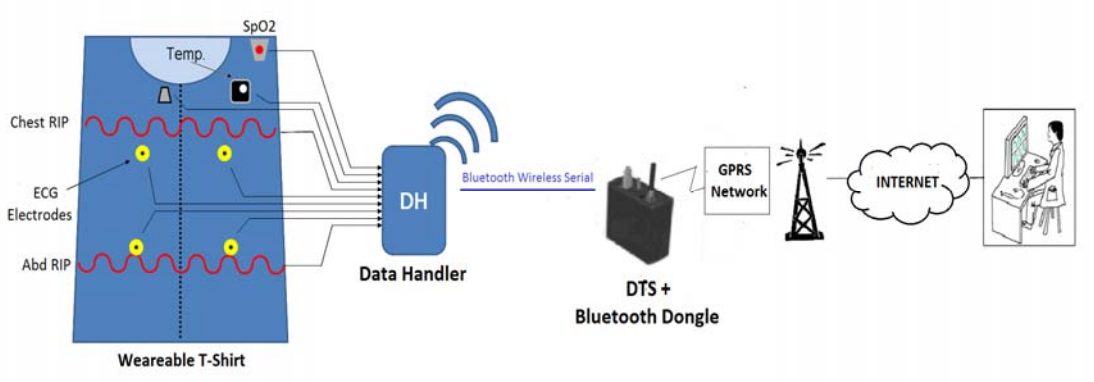


Figure 3.2 - Basic Architecture of wearable T-shirt integration on HMVMS

By the DTS, the data from the t-shirt are sent on the internet via the GPRS network and at the end point can be visualized on real-time by the specialist, together with the data sent by the HMVMS.

In this way, the remote titration can be set up also considering information that figures out from the wearable signal visualization.

Figure 3.3 shows a schematic view of the whole system resulting from the integration of the shirt with the HVMVS:

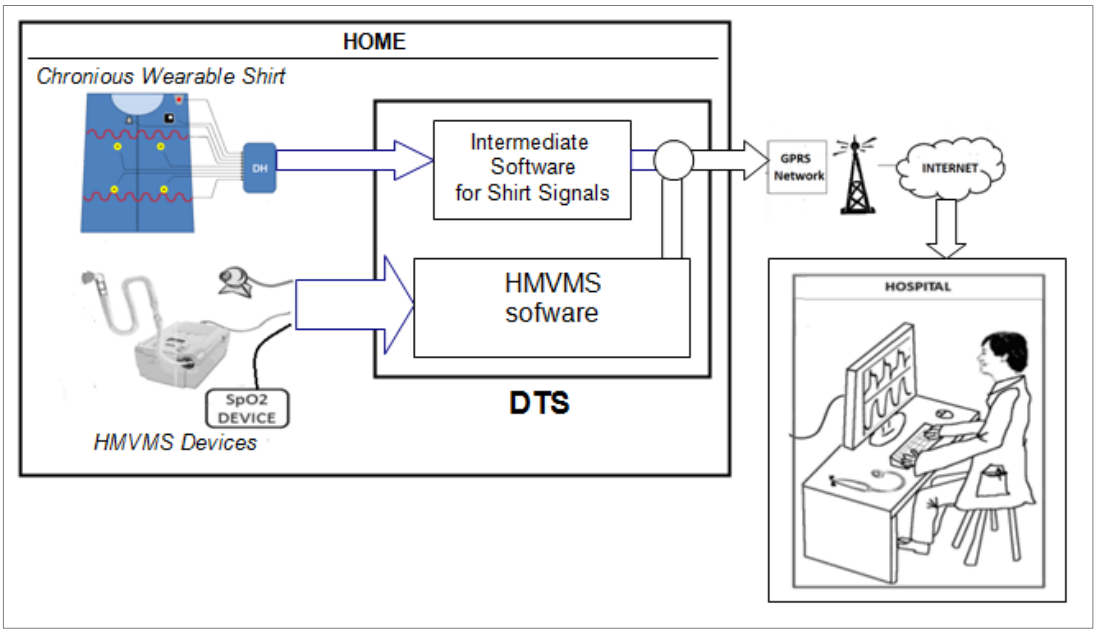


Figure 3.3 - Schematic view of the complete system: HMVMS + Chronious Shirt

To realize such system, it's necessary to implement an intermediate software which takes the data from the Chronious shirt sent by DataHandler over the Bluetooth communication, and transmits them on the Internet in a reliable and fast way.
The intermediate software should be executed together with the HMVMS software on the DTS installed at patient's home, and a remote application on the specialist's station, should permit the final real time visualization of signals.
This chapter will show and discuss in the first part the hardware specifications of the devices used in the project, and in the second part the software solutions adopted to implement the intermediate software and the remote visualization application mentioned above, in order to integrate the Chronious wearable platform in the HMVMS.

3.2 Hardware description

3.2.1 Technical Specification of the DTS

The Data Transfer Server (DTS) is the core of the HMVMS and is made of 3 main components (Figure 3.4).

1. an embedded system board, the FOX board LX 832
2. a GPRS modem comprised in the FOX Board GPRS toolkit
3. a ZigBee (IEEE 802.15.4-2003) module (XBee, MaxStream, DIGI, Minnetonka, Minnesota, USA) that provides a point-to-point wireless serial communication with microcontroller (Microchip, dsPIC30f3013) connected to a standard commercially available pulse oxymeter.

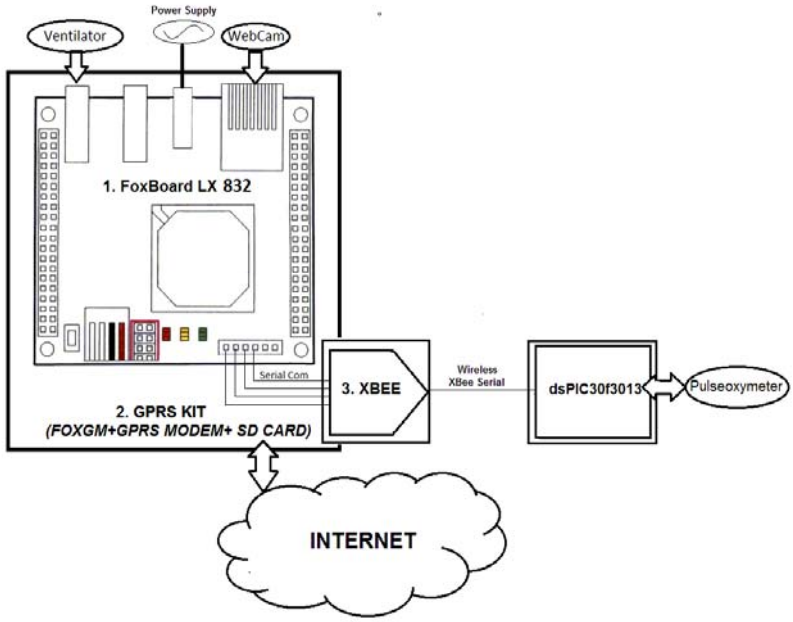


Figure 3.4 - Global Structure of the DTS:

1. Fox Board LX 832 2. GPRS KIT (FoxGM+GPRS MODEM+ SD Card) 3. Zigbee

The **FOX Board** is an embedded board produced by ACME SYSTEM Srl Roma Italy, based on a ETRAX 100LX 100 MIPS RISC microprocessor with 16 MB of RAM and 8 MB of flash memory, 2 USB 1.1 ports, two serial ports and one Ethernet (10/100Mb/s) adapter.

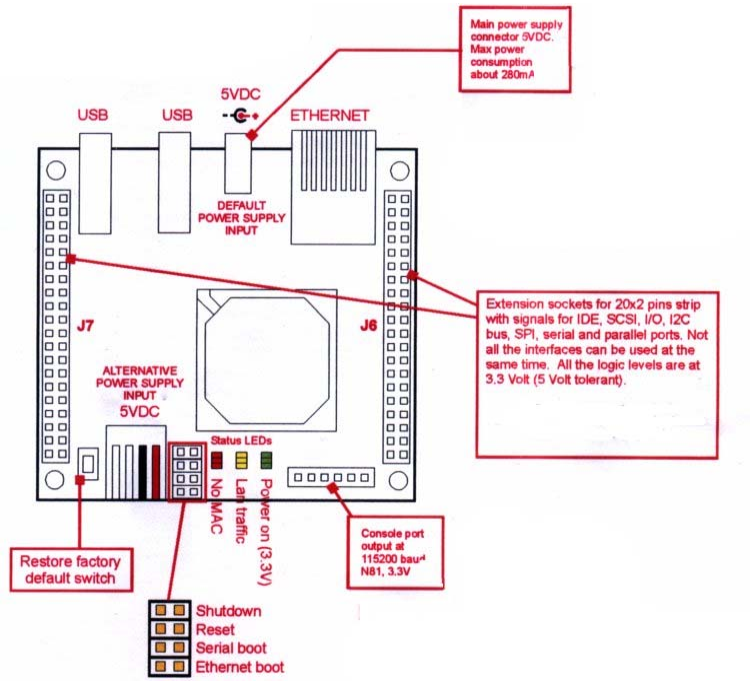


Figure 3.5 - FOX BOARD LX832

It runs an embedded Linux operating system and the full development system is freely available on Internet.

The board represents a small power saving device, particularly indicated for remote multitasking applications that requires data storage and low-level hardware communication.

The presence of Web servers and TCP/IP protocols installed in the OS packages permits the boxboard to behave like a little web station that can connect to the internet.

The connection to the internet can be provided by the GPRS modem part of the Fox Board GPRSKIT (Figure 3.6).

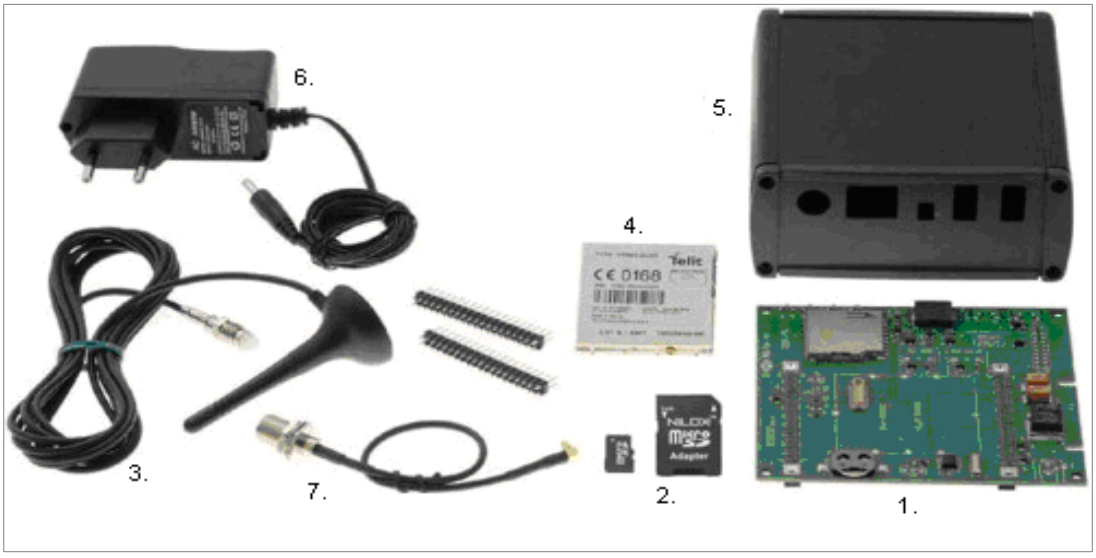


Figure 3.6 - GPRSKIT 1. Fox GM 2 SD Memory Card 3. GSM Antemnae 4.GPSR/GSM Modem 5. Allumium Case 6. Power Supply Adapter 7. Accessories

The Fox Board GPRS kit is a special kit, designed for telecommunication uses of Fox board.

Referring to Figure 2.12, the kit is composed by:

1. *FOX GM,* an additional board that allows the connection between the FOX Board and the GPRS modem: it also contains a Real Time Clock with a back-up batter, a buzzer, and a socket for SD/MMC cards. The connection with Fox board is realized through the J6 and J7 pin sets (see also Fig.2.7)
2. *A Standard SD flash memory card (1 GB)* is *used* for data storage.
3. *GSM omnidirectional antennae,* with quad-band support working on 800/900/1800/1900 MHz frequencies, allowed to be plugged with SMA connector
4. *a GSM/GPRS modem (*Telit GM862-QUAD), with SIM support which uses 3 TDMA time slots for download and 2 for upload, providing a maximum bit rate of 40 Kbps and 60 Kbps.

The Fox board and the GPRSKIT are assembled in a small and lightweight aluminium case unit (figure 2.12 pt.5) whose external dimensions are 110x106x46 mm.

The third part of the DTS, which is the *ZigBee module* (XBee, MaxStream, DIGI, Minnetonka, Minnesota, USA), provides a point-to-point wireless serial communication with a microcontroller (Microchip, dsPIC30f3013).

The microcontroller is a part of a device that is connected and supplies a standard

commercially available pulseoxymeter (XPOD Module, NONIN Medical inc., Plymouth, Minnesota, USA). It is applied at the index finger of the patient and samples patient oxygen saturation (SpO2) and heart rate signals.

The microcontroller sends the data sampled to a ZigBee module that implement a direct serial communication with the DTS.

The microcontroller and the ZigBee module are supplied by a 6V 2400mAh battery and enclosed in a small plastic box: they are held in a power saving functioning modality for about 4 seconds. After this time they activate, sample and send the pulse oximetry data to the DTS in about 0.5 seconds.

This procedure is performed to save power consumption and increase battery life.

The DTS exchanges data with a mechanical ventilator connected through a standard USB port of the Fox Board (ventilation signals, sampled at frequency of 20Hz, from the ventilator to the DTS, and ventilator control signals from the DTS to the ventilator.

DTS is also connected through the Ethernet port to an IP webcam (Foscam FI8918W IP Camera).

The webcam is capable of capturing snapshot in daylight and night-time light thanks to a crowd of infrared leds around the lens and permits a controlled move of the optic group thanks to a step motor installed in.

It is used to take pictures of the patient when requested by the operator.

When the DTS is switched on, it starts sampling and recording the data coming from the ventilator and from the SpO2 device.

At the same time the DTS connects to Internet and activates a server that is ready to accept client connections.

Every single remote DTS can be identified by assigning it a symbolic name [121].

When a physician wants a connection to the patient's ventilator, he has to run a program installed on any computer connected to Internet.

The program asks for the symbolic name of the patient's device and for authentication information. Once the physician is authenticated he can ask for real-time or previously recorded data.

With this approach, only digital signals are transmitted via the GPRS line and no personal patient information is sent or even stored in the telemetric device, thus significantly reducing any concerns about data protection and privacy matters.

Moreover, digital signals are sent via a proprietary binary protocol, making any kind of data sniffing even more difficult.

Physician's computer and the DTS are both authenticated through a Public Key based procedure.

The DTS starts sending the requested data, which are showed in a graph (Figure 2.3 A.), encoded through an Open SSL cryptography protocol.

In every moment the physician can request a snapshot of the patient just clicking on a button on the right corner of the software.

When the request is done, the DTS takes a frame from the webcam and sends it through the Internet to the computer that shows the photography in a dedicated window (Figure 2.3 B).

The program also allows the physician to change the settings of the mechanical ventilator through an apposite menu.

When the physician updates these values on his/her computer, the new settings are transmitted to the DTS and sent in real-time to the mechanical ventilator, after verifying that the new values are within a previously programmed safety range.

3.2.3 The Chronious Wearable system

The Chronius Wearable System is composed of a lightweight and ergonomic designed shirt made of washable stretch-material into which are sewn several sensors for the simultaneous measurement of the following parameters:

- Electrocardiographic activity and heart rate
- Arterial oxygen saturation
- Respiratory activity and respiration parameters
- Body temperature
- Ambient temperature and humidity
- Audio Signals for cough and snoring detection
- Motion and fall detection

For this thesis work, only the first five are used, so audio and fall detection signals and won't be further considered.

The data coming from the sensors are collected and transmitted via a wireless connection through the Bluetooth protocol by the *Data Handler*, a microcontroller-based acquisition system (Figure 3.7).

The aim of the system is to infer complex information about the user's state, the situation around him, and his interactions with the environment.

These unobtrusive wearable sensors will allow monitoring of physiological parameters to be conducted over a period of time directly from patient home.

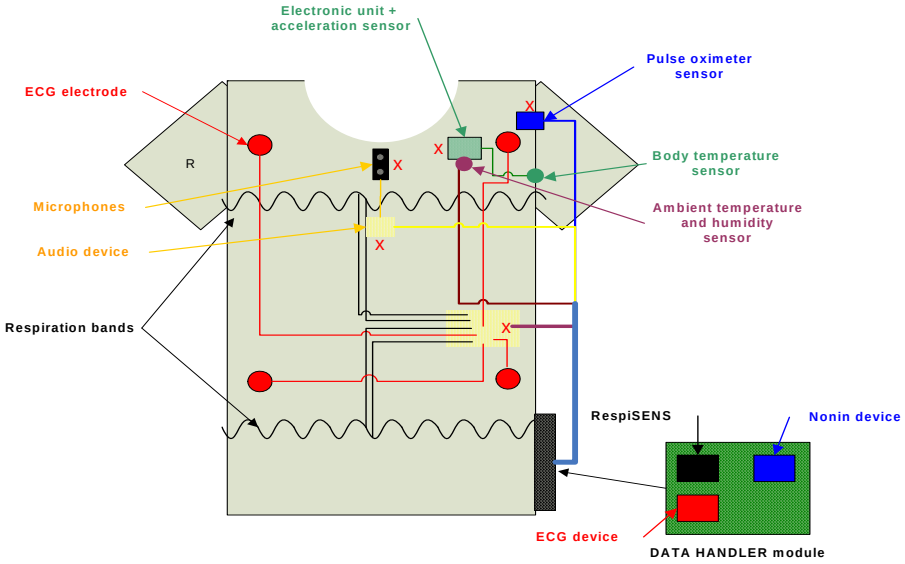


Figure 3.7 - Schema of the Chronius Wearable system: the T-shirt with integrated sensors and Data Handler module.

3.2.3.1 The Chronius wearable T-shirt and the sensors

The Chronius wearable shirt (Figure 3.8) is made up by 8% of elastane and 92% of cotton. It is machine washable at 30°, however the electronic unit and the sensors attached via the hook and loop fasteners must be removed before washing.

The shirt is realized tight enough in order to permit the measurement of the vital parameters and included a central zip to make users easier the wearing of.

It provides also a pocket on the front side, where the Data Handler can be stored in an easy and accessible way for old and obese people.

Due to the high extensibility of the Shirt only three different sizes are provided (S/M and L/XL and XXXL) (see Appendix for shirt specification).

The electrocardiographic signal (ECG) is acquired by means of four dry silver electrodes

that are clipped inside the T-Shirt to gain a total of three ECG derivations, according to the Einthoven's triangle (see Figure 3.8).

Figure 3.8 - T-shirt with the Einthoven triangle and its lead:Lead I: LA – RA, Lead II: LL – RA, Lead III: LL – LA.

The arterial oxygen saturation and the heart rate are measured through the pulseoximetry technique. A pulseoximetry reflectance sensor was used.

The pulseoximetry sensor is an optical front-end that includes a photo sensitive part and a light emitting one.

In particular, the photo sensitive part is a photodiode (PD) and the light emitting part consists of two adjacent light emitting diodes (LED), one emitting red light and the other that can be.

In the reflection sensor selected (Nonin type 8000R, Figure 3.9), PD and LEDs are adjacent: the sensor is placed inside the t-shirt over the left shoulder.

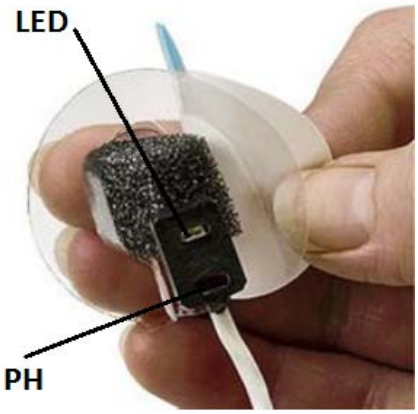


Figure 3.9 - Nonin 8000R reflectance pulsioxymetry sensor

The respiratory activity and the respiratory parameters are measured by means of two inductive bands of insulated electric wire sewn into the shirt (Figure 3.10)

They are placed around the rib cage under the armpits and around the abdomen over the belly bottom.

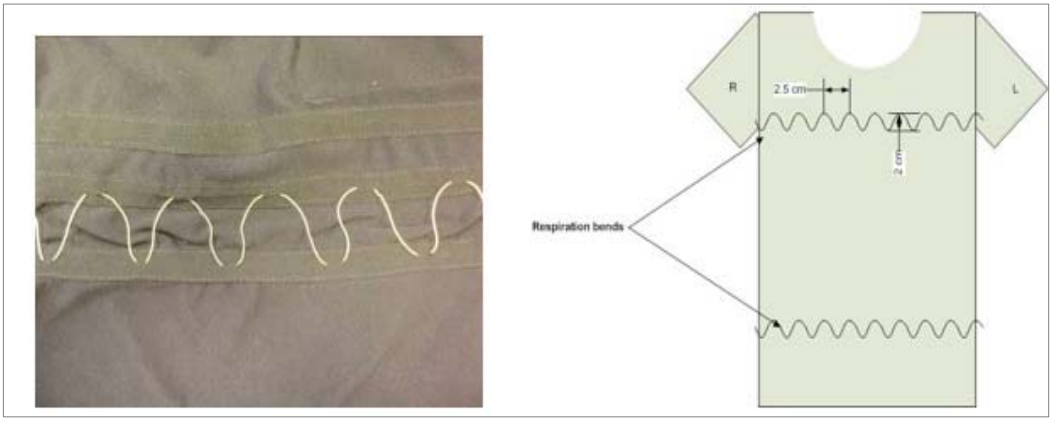


Figure 3.10 - Inductive bands

The two respiratory bands are designed to measure the thorax and the abdomen volume displacement signal by means of the respiratory inductive plethysmography technique (RIP).

Respiratory Inductive Plethysmography (RIP) is a technique able to measure lung volume changes and breathing movements without any connections at the airway opening.

RIP uses inductance coils to measure the respiratory excursion of the ribcage and abdomen.

Each coil is connected to an oscillator module that produces a sine wave of approximately 20mV of amplitude and at a frequency of 930 kHz and 850 kHz, respectively for thorax and abdomen's coil.
This module is in turn connected to a demodulator unit which outputs signals proportional to the cross-sectional area of each coil (Figure 3.11).

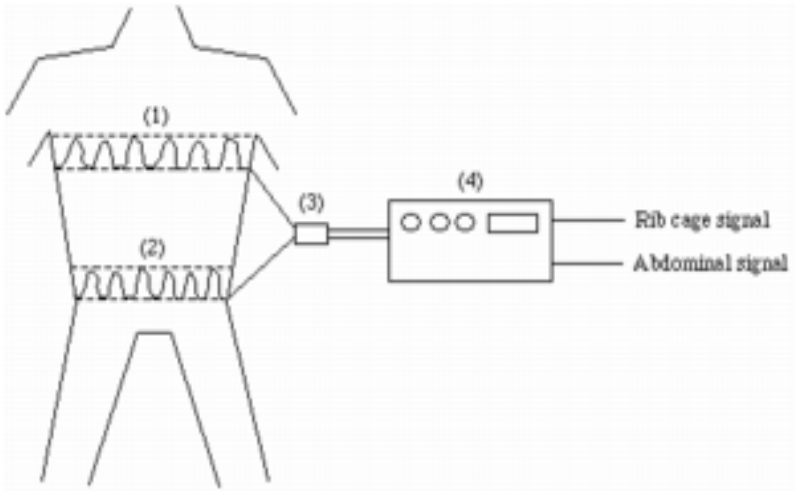


Figure 3.11 - The respiratory inductive plethysmography system including the rib cage (1) and abdominal (2) sensor bands, the oscillator (3), and the signal demodulator (4)

The respiratory system is assumed to be divided in two parts that move with two degrees of freedom (Konno and Mead) [51]. Changes in cross-sectional area of each compartment produce variations in self-inductance of the wire, thereby changing frequency.
This frequency change is demodulated to produce an analog voltage corresponding to waveforms of ribcage and abdomen compartmental volumes as they change during respiration [129].
The weighted sum of the ribcage and abdomen is therefore proportional to the tidal volume (V_T).
The use of RIP needs usually a previous process of calibration to derive the relative contribution of the RC and ABD to the tidal volume.
Whereas, uncalibrated RIP is a valuable means of assessing both respiratory timing and various qualitative aspects of ribcage and abdomen asynchrony [129].

The body temperature is measured by means of the TSic-716 digital temperature sensor of the IST AG (Wattwil, Switzerland), placed on the internal side of the shirt near the left armpit.

TSic 506F as the following characteristics:

- Measurement range: -10-60°C
- Absolute accuracy: +/- 0.1°C
- Resolution: +/- 0.034°C
- Digital output

The ambient temperature and humidity is measured by the SHT75 temperature/humidity sensor of SENSIRION AG (Staefa, Switzerland) placed on the external side of the shirt

This sensor offer following features:

- Measurement range: 0-100% RH
- Absolute RH accuracy: +/- 2% RH
- Repeatability RH: +/- 0.1% RH
- Temp. accuracy: +/- 0.3°C

Calibrated & digital output (2-wire interface)

Both of the sensors are connected to a controller unit implemented on a 34×34×6mm3 custom designed PCB (Figure 3.12).

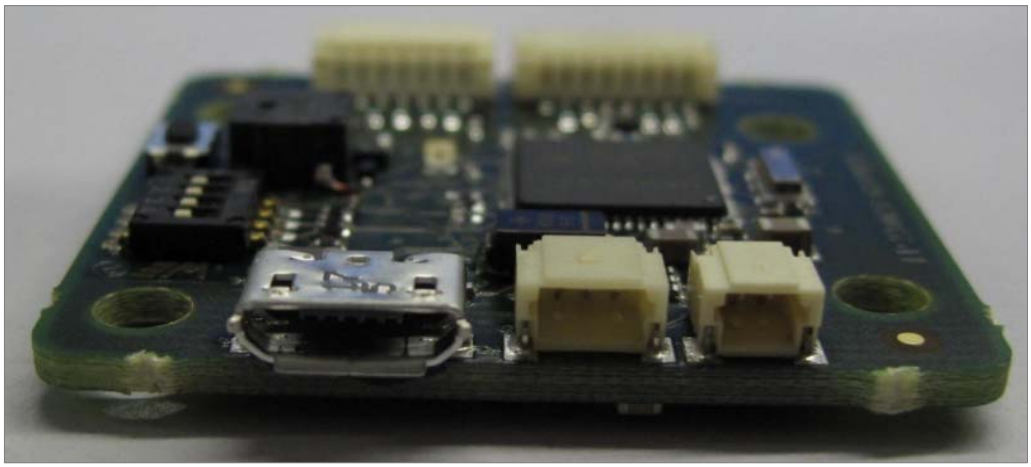


Figure 3.12 - The controller unit

The controller is connected through a microUSB plug to the Datahandler for data transmission and power supply.
It is designed to be fitted into a textile bag made out of a flexible material.
The bag possesses a Velcro pad on its backside as shown in Figure 4-26 on the right-hand side. The shirt has a Velcro counterpart placed on the right upper side.
The attachment is provided by a gentle pressure onto the bag (Figure 3.13).

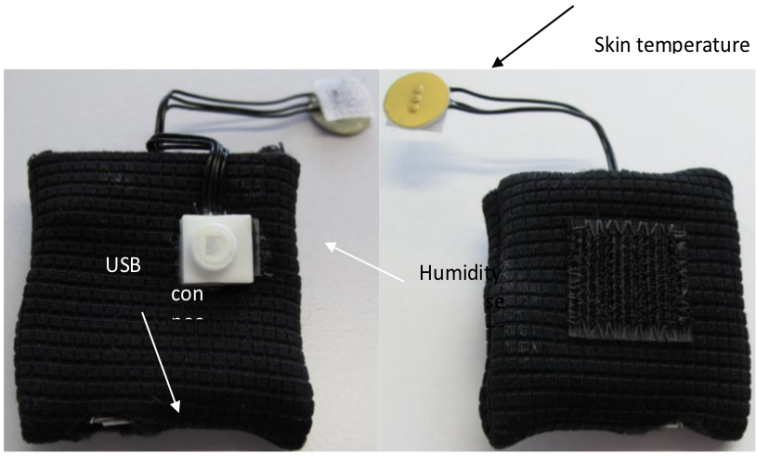


Figure 3.13 -.Photograph of the sensor system. Left: front view with the temperature/humidity sensor. Right: back view with the Velcro attachment to the shirt.

The ambient temperature/relative humidity is placed under a protective cap on the front side of the textile bag.
There is an opening in this cap covered by a humidity transparent material to allow for an undisturbed measurement.
The skin-temperature sensor is connected via a cable to the controller electronics.
The sensor chip is soldered onto a round PCB with a gold-plated ground plain providing thermal contact to the sensor.
The chip itself is hermetically sealed by epoxy, which also holds another Velcro pad.
This Velcro pad allows for the attachment of the skin-temperature sensor to the inner part of the shirt where a counterpart is located.

3.2.3.2 The Data Handler

The Data Handler (DH) is a small electronic device (Figure 3.14) which is responsible for data acquisition, processing and transmission of the signal sensed from the patient body.

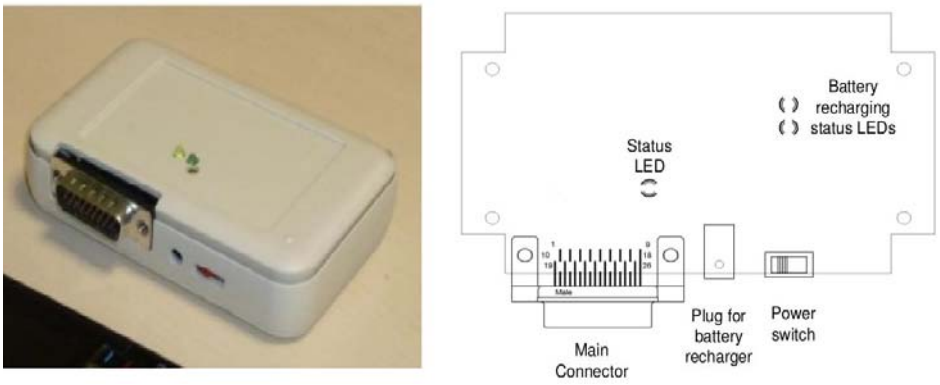


Figure 3.14 - The Data Handler (left) and its user interface (right)

The Data Handler acts as the unique gateway of the shirt sensing elements with the external world and its main actions are:

- Data acquisition and storage
- Data pre-processing and filtering
- Data transmission
- Alerts triggering, based on certain circumstances and signal conditions
- Sensors periodical control of functionality and communication (malfunction detections and report event generation)

Each sensor unit on the shirt provides control processing element which undertakes the role of gathering sensor analogue data, convert them and finally transmit them via a predefined interface to the Data Handler main processor (Texas Instrument TI, MSP430F5438, Figure 3.15).

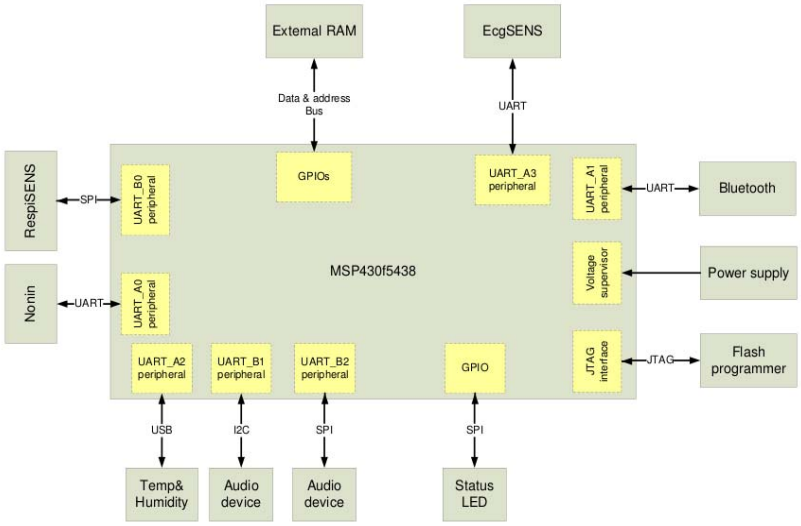


Figure 3.15 - General overview of the DH main processor (TI,MSP430F5438)interfaces.

The Data Handler send data externally using an integrated Bluetooth class 2 module from Stollmann GmbH. This device is small (22.75x13.5x2.85 mm), power saving (8mA in idle and 41mA in transmission) and offers a Serial Port Profile (SPP) compatible with most of the operative systems running on mobile and desktop device; moreover it provides a UART interface to the DH main processor. The Data Handler is powered by a flat rechargeable Lithium-Polymer battery (LPP 503759) produced by Varta AG (Figure 3.16). It is a 3.7V single cell battery having a typical capacity of 1400 mAh that allows a continuous use of the DH V2.0 up to 17.5 hours. The battery (59x37x5 mm) is integrated inside the DH plastic enclosure.

Figure 3.16 - Li-Po battery LPP 503759 by Varta AG

For ECG, Respiration and Reflection sensor modules, the corresponding processing elements are hosted directly to the Data Handler's main board.

They are shown in Figure 3.17 are respectively the electrocardiographic device (EcgSENS), the respiratory device (RespiSENS), and the NONIN OEM III device.

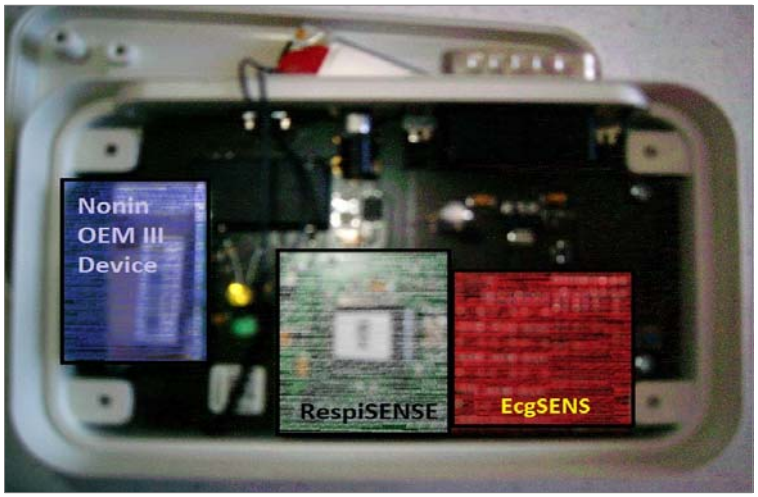


Figure 3.17 Overview of the Data Handler Main Board with the EcgSENS(red),RespiSENS(grey) and Nonin OEM II processing units(blue)

The electrocardiographic device (EcgSENS) for the acquisition of the ECG signals is an embedded system based on a microcontroller of the Texas Instruments.

The EcgSENS hardware includes three processing blocks (Figure 3.18).

The first block represents the electrical impedance adjustment of the signals acquired from the electrodes.

The second block provides a pre-processing of the signal by means of instrumentation amplifiers. The use of the driven right leg circuit permits the reduction of the common mode noise.

The third block is a set of 8th order analogue low pass filter, one for each channel, and an external digital analogue converter.

The last block represents the microcontroller unit including the CPU, the RAM and E2PROM, the internal analogue to digital converter (ADC), UART/SPI peripherals and I/O pins.

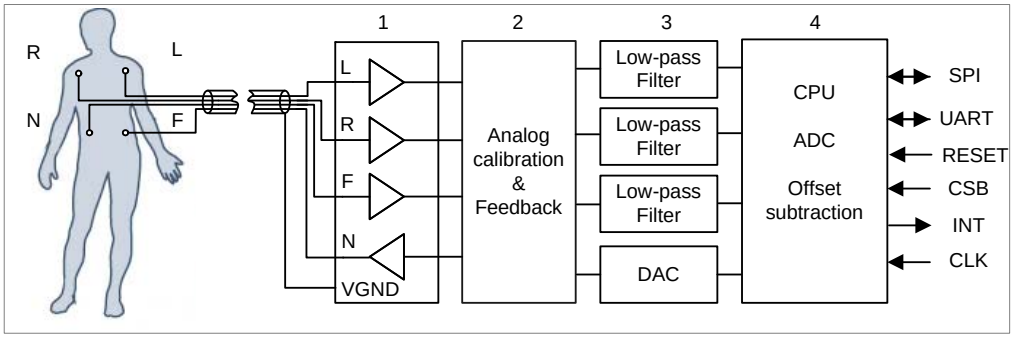


Figure 3.18 -: The ECG device block diagram.

The transferred data to the microcontroller unit are the three electrocardiographic derivations signals. The microcontroller sent a continuous stream of these data at a sampling rate of 256 Hz.

The RespiSENS device has been developed by the Fraunhofer Institute for Integrated Circuits IIS (Erlangen, Germany).

RespiSENS is an embedded system based on a microcontroller (Texas Instruments) and is designed to measure thoracic and abdominal volume displacement signal sensed from the two integrated coils.

The RespiSENS hardware includes two LC oscillator circuits, an analogue to digital converter (ADC) and the microcontroller unit (Figure 3.19).

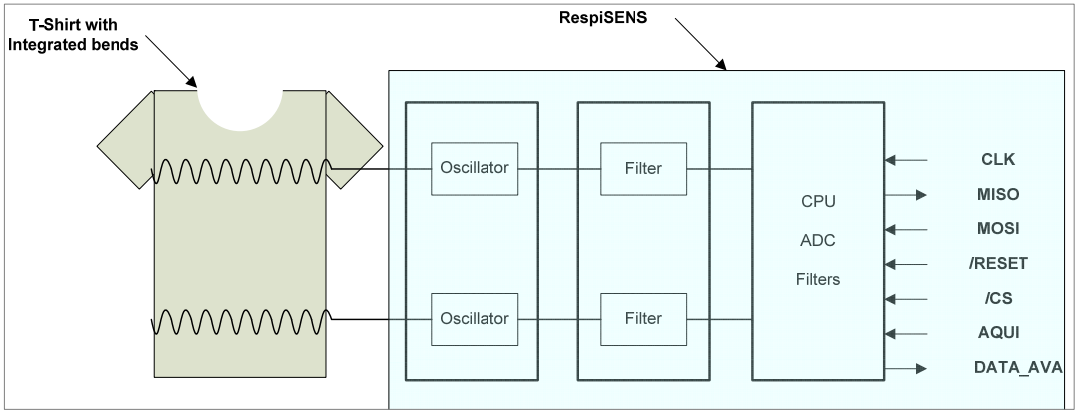


Figure 3.19 - RespiSENS block diagram.

The microcontroller sent a continuous stream of data of thorax and abdominal volume displacements at a sampling rate of 12,5 Hz.

NONIN OEM III Module measures the oxygen saturation, the heart rate and the perfusion index by means of one reflectance sensor frontend.

The data generated by NONIN OEM III are:

– Oxygen saturation: range 0 to 100%
– Pulse rate: range 18 to 300 pulse per minute
– Pulse wave: as continuous signal (8-16 bit resolution) 75Hz

The device sent a continuous stream of data at a sampling rate of 1 Hz.

Contrary to previous, the controller unit for temperature and humidity sensors is hosted in a separate board (cfr paragraph 3.2.3.1) placed in a textile bag located near the left armpit.

Figure 3.20 shows the block diagram of the controller unit

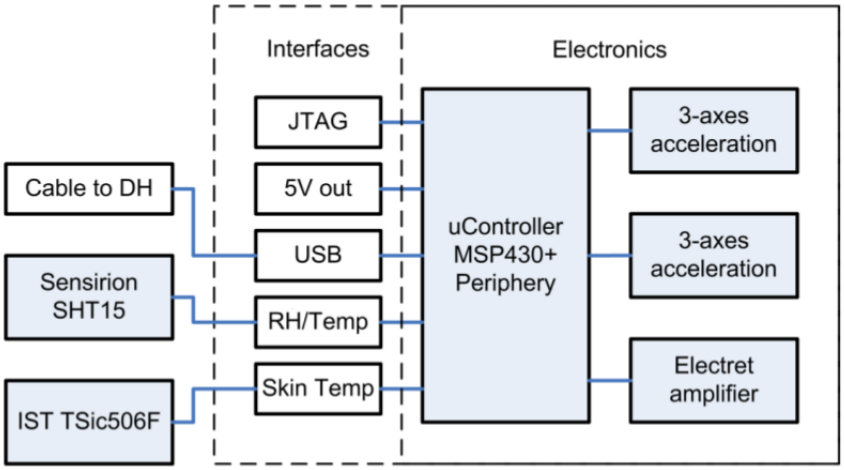


Figure 3.20 - RespiSENS block diagram

The core of the controller unit is the MSP430F1611 microcontroller of Texas Instruments.

The periphery of the microcontroller consists of an FTDA serial-to-USB bridge, a buzzer circuitry, a real-time clock (RTC), and an electret amplifier.

The USB connection is intended to provide the circuitry with the power from the data handler and to transmit the measured data.

The buzzer is implemented to provide an acoustic-alarm probability if needed.

RTC provides clock-frequency signal to the microcontroller and the optional amplifier can be used to process an analogic audio signal from an external electric microphone.

The controller unit samples the signals for the temperature and humidity sensors once a minute, at a sampling frequency of 0,016 Hz.

3.2.3.3 Connection between the Shirt and the Data Handler

The signals, acquired from integrated sensor modules on the shirt, are transferred directly

to the Data Handler via a unique cable

The cable is connected on one side through the connector S1 to the Data Handler

The connector S1 is a high density sub-miniature D connector with 26 poles (Figure 3.21).

Figure 3.21 - sub-miniature D connector

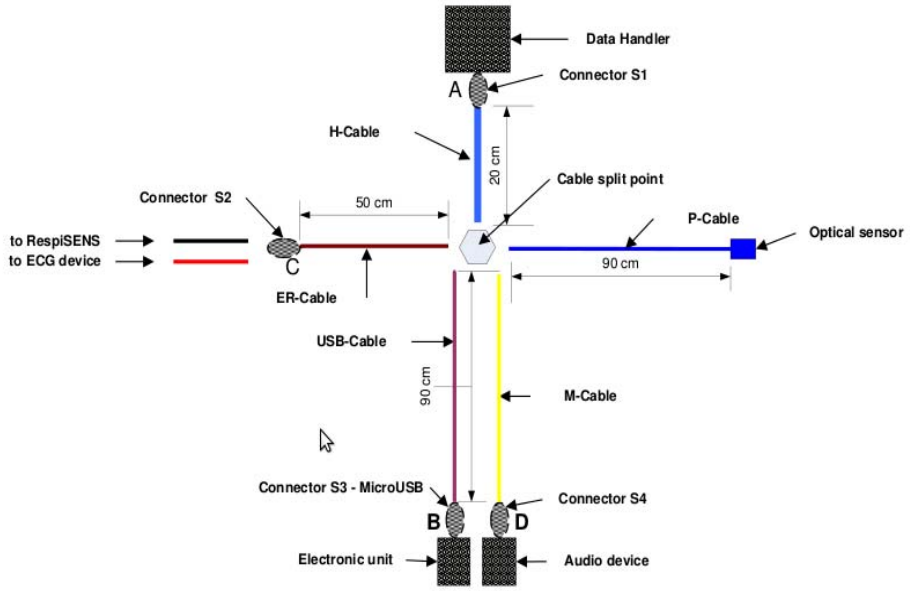


Figure 3.22 - Schematic view of the cable and its connectors

On the other side the cable splits to four different parts (Figure 3.22).

The P-cable host the reflection sensor of the pulse oximeter and transmits two control signals for the leds, one analogue signal from the photodiode and one for the sensor type detection.

The ER-cable is plugged through the connector S2 to the respiration bands and to the ECG electrodes integrated in the Shirt. It transmits two analogue signals for the respiration bands and four analogue signals from the ECG electrodes.
The ECG electrodes and respiration band are connected through two special connector with four pins (Figure 3.23)

Figure 3.23 - 4 pins connector of ECG electrodes and respiratory bands

The USB-cable is plugged through the micro-USB connector S3 to the controller unit of temperature and humidity sensors.
The M-cable is plugged through the connector S4 to the audio device via I 2C.

3.2.4 The USB Bluetooth dongle

The wireless connection between the DTS and the Data Handler using the Bluetooth technology has been realized on DTS side through the Nano Bluetooth USB 2.0 dongle by Mediacom (Figure 3.24).

Figure 3.24 - Nano Bluetooth USB 2.0 dongle by Mediacom

This USB dongle permits Bluetooth connections far to 15 m with the v 2.0 protocol.
It's USB 2.0 e 1.1 compatible and runs on Windows Vista, Window 7 and Linux OS

environments.
The Nano Bluetooth USB 2.0 dongle has been chosen for its cheapness and its compatibility with Linux OS: it has been plugged in the second USB plug of the Fox Board LX832 (Figure 3.5) and opportunely interfaces with Linux 2.2 kernel of the board.

3.3 Communication protocols description

In order to integrate of the Chronius wearable sensored shirt with the HMVMS several data communication protocols has been used.
To better understand the software and the firmware implemented for integration, such protocols will be here presented and described.

3.3.1 The RS-232 Serial Communication

Serial communication is a way to allow different devices to communicate.
Serial transmission involves the sending of data one bit at a time, sequentially, over a communication channel or computer bus. Serial link is used also for wireless communication [132].This is in contrast to parallel communication, where several bits are sent as a whole, on a link with several parallel channels.
The serial port is used to convert each byte to a stream of ones and zeroes as well as to convert streams of ones and zeroes to bytes. The serial port contains an electronic chip called a Universal Asynchronous Receiver/Transmitter (UART) that actually does the conversion.
There are two methods for serial communication:
synchronous serial communication, the receiver must know when to “read” the next bit coming from the sender, this can be achieved by sharing a clock between sender and receiver
asynchronous serial communication: asynchronous communication allows data to be transmitted without the sender having to send a clock signal to the receiver.
The RS-232 serial communication protocol is a standard protocol used in asynchronous serial communication that defines **the data to be sent in** words of 8 bits, where the logic 0 (space) values is coded by a positive 2.5 to 12 volt signal and logic 1 (mark) by a negative

-2.5 to -12 volt.

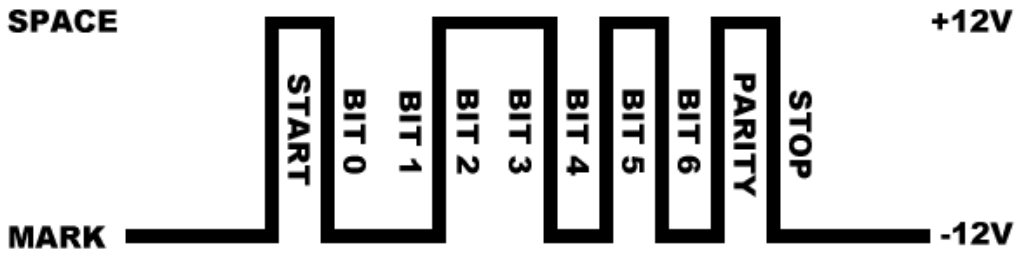


Figure 3.25 - Word of bits in RS-232 Standard

When a word is given for the asynchronous transmission, a bit called the "Start Bit" is added to the beginning of each word that is to be transmitted [132].

The Start Bit is used to alert the receiver that a word of data is about to be sent, and to force the clock in the receiver into synchronization with the clock in the transmitter.

After the Start Bit, the individual bits of the word of data are sent; each bit in the word is transmitted for exactly the same amount of time as all of the other bits

When the entire data word has been sent, the transmitter may add a Parity Bit that the transmitter generates. The Parity Bit may be used by the receiver to perform simple error checking.

Then at least one Stop Bit is sent by the transmitter.

The Baud rate is a measurement of transmission speed in asynchronous communication; it represents the number of bits that are actually being sent over the serial link, including the overhead bits Start, Stop and Parity.

3.3.2 The Bluetooth transmission technology

3.3.2.1 General description

Bluetooth represents an economic and reliable standard method to exchange data at short ranges (from 10 to 100 meters) between several devices with low power consumption and without any cable, using short-wavelength radio transmissions [131].

The Bluetooth technology provides both a point-to-point connection and a point-to-multipoint connection.

Bluetooth protocols assume that a small number of units will participate to communications at any given time.

These small groups are called piconets, and they consist of one master unit and up to seven active slave units within a distance of 10 meters (Figure 3.26).

The master is the unit that initiates transmissions, and the slaves are the responding units. This type of Bluetooth network can have only one master unit.

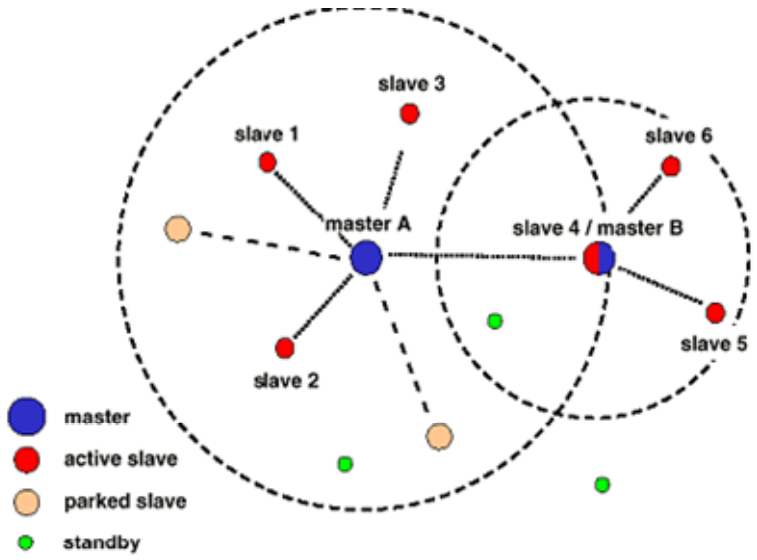


Figure 3.26 - Two piconets forming a scatternet

In addition to the seven active slave nodes in a piconet, there can be up to 255 parked nodes in the net. These are devices that the master has switched to a low-power state to reduce the drain on their batteries. In parked state, a device cannot do anything except respond to an activation or beacon signal from the master. There are also two intermediate power states, hold and sniff, but these will not concern us here.

Any unit in one piconet can communicate in a second piconet as long as it serves as master for only one piconet at a time.
If several piconets overlap a physical area, and members of the various piconets communicate with each other, this new, larger network is known as a scatternet.

3.3.2.2 The Bluetooth protocol stack

The protocol stack makes up the core portion of the Bluetooth implementation.
This stack enables devices to locate each other and establish a connection. Through this connection, devices can exchange data and interact with one another through various applications [131].The Bluetooth specification divides the Bluetooth protocol stack into three logical groups (Figure 3.27).
They are the Transport Protocol group, the Middleware Protocol group and the Application group.

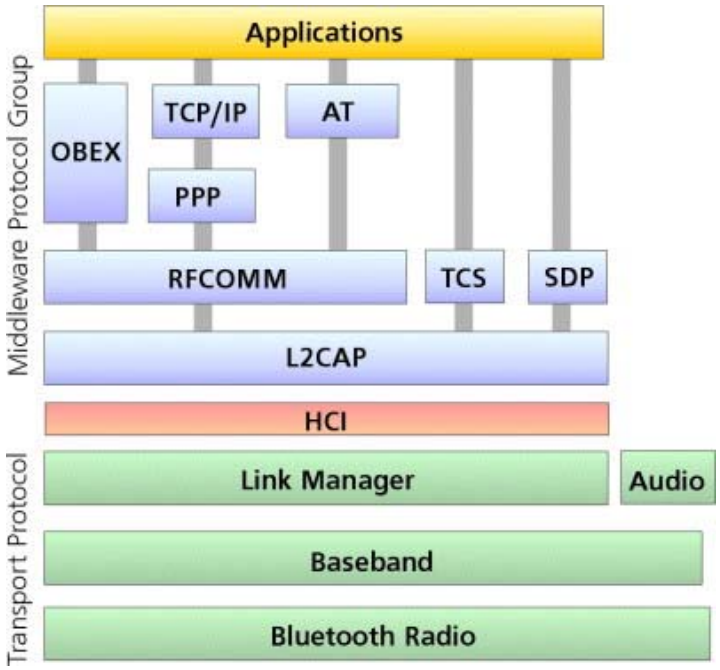


Figure 3.27: Bluetooth Protocol Stack

The Transport group protocols allow Bluetooth devices to locate each other, and to manage physical and logical links with higher layer protocols and applications: these protocols correspond to the Data-Link and Physical layers of the OSI model [130].
The Radio, Baseband, Link Manager, Logical Link Control and Adaptation (L2CAP) layers and the Host Controller Interface (HCI) are included in the Transport Protocol

group.

These protocols support both asynchronous and synchronous transmission.

Radio layer is primarily concerned with and to manage physical and logical links the design of the Bluetooth transceivers, with higher layer protocols and applications.

RF operation uses a shaped, binary frequency modulation to minimize transceiver complexity.

Baseband layer defines how Bluetooth devices search for and does not indicate that it coincides with the connect to other devices. The master and slave roles that a device may assume are defined here, as are the frequency-hopping sequences used by devices.

Also, defined here are the types of packets, packet processing procedures and the strategies for error detection and correction, signal scrambling (whitening), encryption, packet transmission and retransmissions [130].

Link Manager layer, implements the Link Manager Protocol (LMP), which manages the properties of the air-interface link between devices. LMP manages bandwidth allocation for general data, bandwidth reservation for audio traffic, authentication and relationships between devices, encryption of data and control of power usage [131].

Logical Link Control and Adaptation Protocol (L2CAP) supports higher level protocol multiplexing, packet segmentation and reassembly, and the conveying of quality of service information.

HCI layer. The Host Controller Interface (HCI) provides a command interface to the Baseband Link Controller and Link Manager, and access to hardware status and control registers.

The Middleware Protocol group includes third-party and industry-standard protocols, as well as Bluetooth SIG-developed protocols.

These protocols allow existing and new applications to operate over Bluetooth links.

Industry-standard protocols include Point-to-Point Protocol (PPP), Internet Protocol (IP), complex networking Transmission Control Protocol (TCP), wireless application protocols (WAP), and object exchange protocol (OBEX) adopted from Infrared Data Association (IrDA) [130].

Bluetooth SIG-developed protocols include:

the **Radio Frequency Communication protocol (RFCOMM)** provides emulation of serial ports over the L2CAP protocol.

The **Service Discovery Protocol (SDP)** provides a means for applications to discover which services are provided by or available through a Bluetooth device. It also allows applications to determine the characteristics of those available services.
The Application group consists of actual applications that use Bluetooth links.
They correspond to the Application level of the ISO/OSI model.
The knowledge of complete Bluetooth stack is essential for the implementation of application based on Bluetooth technology.

3.3.2.3 The Bluetooth connection

When two Bluetooth devices enter into communication range, they will attempt to communicate with each other. If no piconet is available at that time, a negotiation process will ensue.
One device will become the master (usually the device which initiated the communication) and the other will become a slave: any Bluetooth device can function within a piconet as a master or slave and these roles are temporary and exist only as long as the piconet itself exists.
The master device selects the frequency, the frequency-hopping sequence, the timing of the hop and the polling order of the slaves.
Each Bluetooth device is identified by a unique 12 hexadecimal digit address called Bluetooth address.
Before you can connect two devices via Bluetooth they must be "paired".
Many of the services offered over Bluetooth can expose private data or allow the connecting party to control the Bluetooth device.
For security reasons it is necessary to be able to recognize specific devices and thus enable control over which devices are allowed to connect to a given Bluetooth device. At the same time, it is useful for Bluetooth devices to be able to establish a connection without user intervention, for example, as soon as they are in range.
To resolve such problems Bluetooth technology uses a process called bonding: bond is created through the process of pairing, indeed.
The pairing process aims to create a reliable communication channel between two devices where they share their BT address and their supported profiles: it is triggered either by a specific request from a user to create a bond (for example, the user explicitly requests to

"Add a Bluetooth device"), or it is triggered automatically when connecting to a service where the identity of a device is required for security purposes.

During the pairing process, the two devices involved establish a relationship by creating a shared secret known as a link key, a 128 bit random generated number.

If a link key is stored by both devices they are said to be paired or bonded.

A device that wants to communicate only with a bonded device can cryptographically authenticate the identity of the other device, and so be sure that it is the same device it previously paired with.

From the Bluetooth v2.0 and before, the only secret input to the key calculation is the passkey (PIN): pairing is only successful if both devices furnish the same PIN code.

Any 16-byte UTF-8 string may be used as a PIN code.

When an inquiring device, sends a request of pairing, and PIN number is asked.

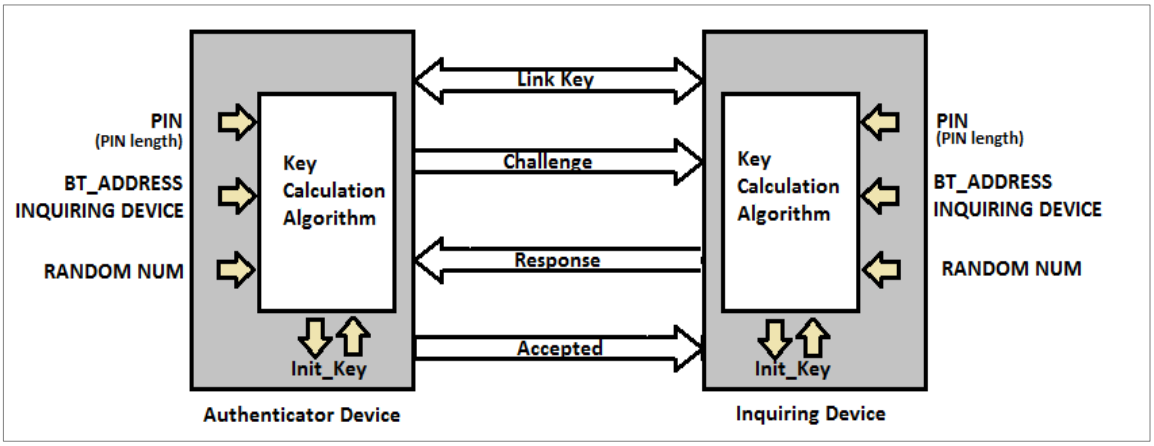


Figure 3.28 - Pairing and authentication mechanism

After PIN exchange correctly the link key is calculated.

This calculation is protected using of an initialisation key, obtained on the basis of the PIN, the Bluetooth address of the inquiring device, the length of the pin code and a random number.

Directly after the exchange of the link key, the authentication procedure is performed with a challenge/response mechanism.

The authenticator sends a challenge using the newly derived link key, and verifies the correctness of the response from the inquiring.

Once pairing and authentication successfully complete, a bond will have been formed

between the two devices and their identity have been confirmed, enabling those two devices to connect to each other.

3.3.3 Data Handler data transmission protocol

The CHRONIOUS Data Handler interacts with the several modules of the wearable shirt with different communication capabilities and requirements.
Besides sensor level communication, Data Handler also acts as a Data Server, transmitting patient's data via wireless Bluetooth technology [128].
As mentioned in earlier paragraphs, RFCOMM protocol, offers a Serial Port Profile over Bluetooth. Data Handler creates a connection with the other devices using the Radio Frequency communication protocol (RFCOMM), providing an emulated RS-232 serial port interface.
Data Handler application configures this interface as any other serial interface.
The communication speed of the Bluetooth communication is defined to 115200 bps (baud per seconds) of Baud-Rate without any parity, 1 stop bit and no hardware/software control.
The DH communicates over RFCOMM sending data frames each one having the following structure (Table 3.1):

Object	Length (bytes)	Description
Start-Byte	1	Start byte used for frame synchronisation
Length	2	Frame length
Timestamp	7	BCD coded
Event	1	Event number
Data ID	1	Data type
Data	…	Depending on data type
Checksum	2	CS1, CS2

Table 3.1: Dataframe structure

Each data frame contains:

- **start-byte**: is used as Start-Byte for frame synchronisation, it's value is for every data frame 0xA8
- **length:** it contains the bytes number of the complete data frame from the start byte to the last checksum byte, coded in a total of two bytes: the first is the LSB (less

significant byte) and the second is the MSB (most significant byte).

LSB	MSB

Table 3.2: Dataframe Length bytes structure

- **timestamp:** the timestamp represents the time at which the data were sampled or generated. The timestamp is BCD coded as follows,

Example: 2008-Nov-10 16:33:59.99

0x08	0x0B	0x0A	0x10	0x21	0x3B	0x63
Year (Hex)	Month (Hex)	Day (Hex)	Hour (Hex)	Minute (Hex)	Second (Hex)	MilliSec (Hex)

Table 3.3: Timestamp bytes structure

- **event number :** the event number identifies different events detected starting with number one. When no event is detected or during real time data sending the value is set to zero. The event number has not been used in the following elaborations so is not further considered.

Data ID	Data type	Data length within a frame	Byte(s) generated per second
0x00	ECG data	6	256 x 3 (channel)
0x02	RespiSENS data	18	12.5
0x03	Pulse oximeter data	2	2
0x05	Temperature and humidity	6	6/60

Table 3.4: Data Handler data ID

- **data ID:** identifies the signal from the data frame comes. Table 3.4 shows Data ID that are used, as the number of bytes used to the core data (data length within a frame) and the number of bytes of the specific type transmitted per second.
- **data:** these are the bytes containing the proper information from the sensor. The number of such bytes as their structure depends on data type. The first is indicated in Table 3.4.

The structure of data byte will be further explain for each data type

- **checksum bytes:** are two bytes used to control the integrity of the data frame. They are calculated as follows :

```
unsigned char CS1 = CS2 = 0
For i = 1 : end
CS1 = CS1 + Byte(i)
CS2 = CS2 + CS1
Next i
```

where Byte(i) is the byte of the data frame starting from the Start-Byte (i = 1) to the last byte before the checksum (i = end).

CS1 and CS2 so computed at the last iteration represent the checksum and are sent with the following order: CS1, CS2.

In order to avoid synchronization problem within the data transmission a byte stuffing algorithm is used.

Byte stuffing is a process that transforms a sequence of data bytes that may contain 'illegal' or 'reserved' values into a potentially longer sequence that contains no occurrences of those values [134].

Since the 0xA8 is used as Start-Byte the following byte stuffing is adopted:

0xA8 -> 0xA9 0x88

0xA9 –> 0xA9 0x89

This means that every 0xA8 and 0xA9 byte occurring within the data frame (including length, time stamp, data or checksum) is replaced with the aforementioned pair of byte.

3.3.3.1 ECG data structure

ECG data are identified with Data ID 0x00 and contain three channels ECG signals generated from EcgSENS at 256 samples per seconds (256 Hz). Each channel has 16 bits (2 bytes) resolution codified as unsigned int, therefore six bytes are sent in each data frame according to the following structure:

CH1 (LSB)	CH1 (MSB)	CH2 (LSB)	CH2 (MSB)	CH3 (LSB)	CH3 (MSB)

Table 3.5: ECG data Structure: MSB=most significant byte LSB=less significant byte

CH1(LSB) is the first byte to be sent, CH1(MSB) is the second, CH2 (LSB) is the third and so on.

CH1 is, according to the Einthoven triangle, the LA-RA (left arm – right arm) lead.

CH2 is, according to the Einthoven triangle, the LL-RA (left leg – right arm) lead.

CH3 is, according to the Einthoven triangle, the LL-LA (left leg – left arm) lead.

3.3.3.2 RespiSENS data structure

The RespiSENS data are identified with Data ID 0x02 and are 18 bytes generated 12.5 times per second (12,5 Hz).

Together with the inductive band signals, there are transmitted other data calculated by the RespiSENS microcontroller on the basis of firsts.

Data are encapsulated according to the following table:

1st	2nd
Thorax (LSB)	Thorax (MSB)
Abdomen (LSB)	Abdomen (MSB)
Tidal volume (LSB)	Tidal volume (MSB)
Breath amplitude (LSB)	Breath amplitude (MSB)
Minute ventilation (LSB)	Minute ventilation (MSB)
Breathing rate / tidal volume (LSB)	Breathing rate / tidal volume (MSB)
Labour breathing index (LSB)	Labour breathing index (MSB)
Breathing rate	Inspiratory time
Expiratory time	Inspiration/expiration

Table 3.6: RespiSENS data Structure: MSB=most significant byte LSB=less significant byte

Thorax (LSB) is the first byte to be sent, Thorax (MSB) is the second, Abdomen (LSB) is the third and so on.

Thorax is the calibrated thoracic displacement volume in ml.

Abdomen is the calibrated abdominal displacement volume in ml.

Tidal volume is the sum of the calibrated thoracic and abdominal displacement volume in ml.This first three are transmitted as the two's complement value of the correct measure.

Table 3.6 shows their range:

Data	Resolution	Range	Data type	Note
Calibrated thorax volume displacement	16 bits	-32767 – 32767	Signed int (two's complement)	Millilitre
Calibrated abdomen volume displacement	16 bits	-32767 – 32767	Signed int (two's complement)	Millilitre
Tidal volume	16 bits	-32767 – 32767	Signed int (two's complement)	Millilitre

Table 3.7: RespiSENS data range

Breath amplitude is the breath amplitude calculated from the tidal volume signal in ml

Minute ventilation is the breath rate times the breath amplitude in ml.

Breathing rate / breath amplitude is the computed breath rate over the breath amplitude multiplied by 1000 (e.g. 0.015 (bpm/ml) is coded as 15).

Labour breathing index is the computed value times 100 (e.g. 102 (LBI) is coded as 1.02).

Breathing rate is the computed breathing rate per minute.

Inspiratory time is the computed value in step of 80 ms (e.g. 800 ms is coded as 10).

Expiratory time is the computed value in step of 80 ms (e.g. 800 ms is coded as 10).

Inspiration/expiration is an index that is used to recognize one breath from another, set to 1 when inspiration occurs and to 0 when expiration occurs.

These lasts are not further considered in the following elaborations.

3.3.3.3 PulsiOximeter data structure

The pulse oximeter data are identified with Data ID 0x03 and are two bytes generated once per second (1 Hz). Data are encapsulated according to the following table:

Bit 7	Bit 6	Bit 5	Bit 4	Bit 3	Bit 2	Bit 1	Bit 0
HR8	HR7	HR6	HR5	HR4	HR3	HR2	HR1
HR0	SP6	SP5	SP4	SP3	SP2	SP1	SP0

Table 3.8: PusiOximeter data structure

HR8-HR0 are the bits of the heart rate value.

SP6-SP0 are the bits of the oxygen saturation value.

3.3.3.4 Temperature and humidity data

Temperature and humidity data are identified with Data ID 0x05 and contain 6 bytes generated once per minute (0,016 Hz) .The transmitted data are:

Ambient humidity (LSB)	Ambient humidity (MSB)	Ambient temperature (LSB)	Ambient temperature (MSB)	Skin temperature (LSB)	Skin temperature (MSB)

Table 3.9: Temperature and Humidity sensors data structure

Ambient humidity (LSB) is the first byte to be sent, ambient humidity (MSB) is the second, ambient temperature (LSB) is the third and so on.

3.3.4 The Transmission Control Protocol (TCP)

The Transmission Control Protocol (TCP) is one of the core protocols of the Internet Protocol Suite.

TCP is one of the two original components of the suite, complementing the Internet Protocol (IP), and therefore the entire suite is commonly referred to as TCP/IP [136].

TCP is known as a connection-oriented protocol, which means that a connection is established and maintained until such time as the message or messages to be exchanged by the application programs at each end have been exchanged.

In the Open Systems Interconnection (OSI) communication model, TCP is in layer 4, the Transport Layer [135].

TCP establishes a full duplex virtual connection between two endpoints or sockets.

A **socket** is an endpoint of an inter-process communication flow across a computer network.

Each socket is defined by an **IP address** and a **TCP port number**.

As many ISO/OSI protocols, TCP respects a **client-server** architecture.

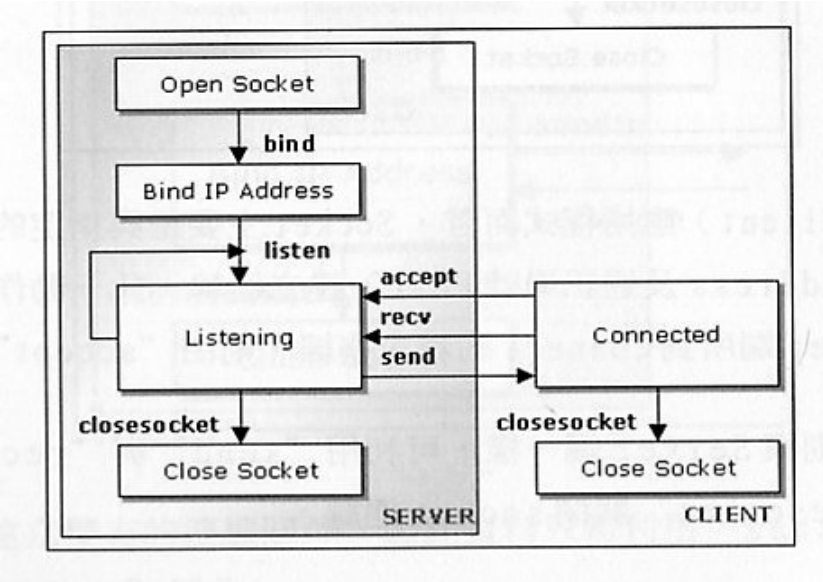


Figure 3.29 - Client-server architecture

Computer processes that provide application services are called servers: they create sockets, bind them to the server IP address and keep them in listening state.

These sockets are waiting for initiatives from client programs.

A client initiate application data transfers using TCP, knowing the IP of the server and the port number that identifies servers, that is trying to reach the server socket.

Servers can accept client request, starting the data sending.

A TCP server may serve several clients concurrently, by creating a child process for each client and establishing a TCP connection between the child process and the client. Unique dedicated sockets are created for each connection. These are in established state, when a socket-to-socket virtual connection also known as a TCP session, is established with the remote socket, providing a duplex byte stream [136]. A server may create several concurrently established TCP sockets with the same local port number and local IP address, each mapped to its own server-child process, serving its own client process. They are treated as different sockets by the operating system, since the remote socket address (the client IP address and/or port number) are different.

Client and server sockets can be closed, and the connection drops down.

If a client socket is closed the correspondent server socket can return in listening state.

TCP is responsible for ensuring that a message is divided into the packets and transmitted

as stream of octets at the source. It manages also for reassembling the packets back into the complete message at the other end.

TCP provides many services such as data reliability, error checking, and flow control. If a data packet is corrupt or lost (not acknowledged), TCP will retransmitted the data from the client side automatically.

Because the route a packet takes can be many, one packet may arrive before the one sent earlier. As data packets arrive, it is the job of TCP to assemble the packets into the proper order.

Figure 3.30 show a TCP Header for example:

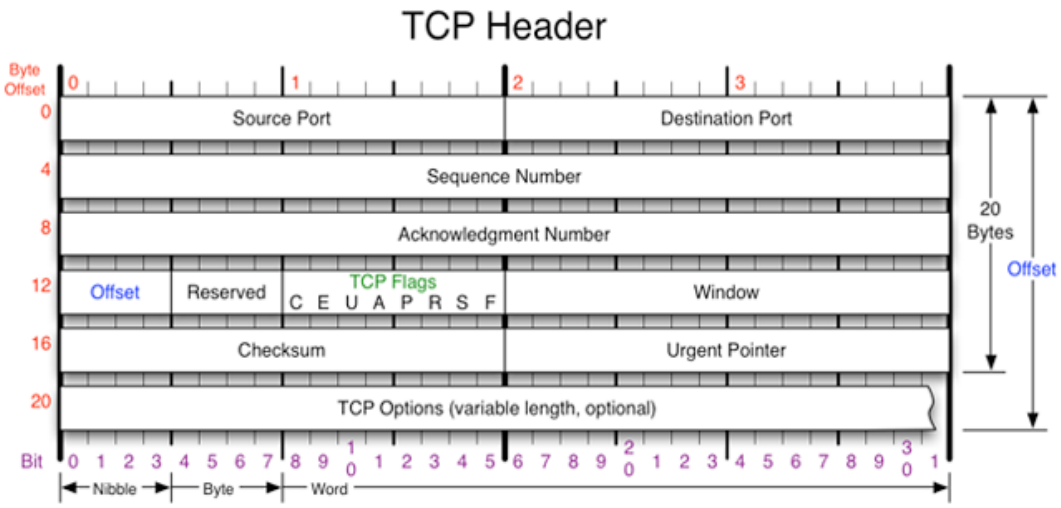


Figure 3.30 - TCP Header

TCP uses data sequence numbering to identify packets, and explicit acknowledgements numbers (ACKS) to allow the sender and receiver to be aware of reliable packet transfer. This form of reliable protocol design is termed "end-to-end" control, because interior switches do not attempt to correct packet drops. Instead, this function is performed through the TCP protocol exchange between sender and receiver.

TCP also uses ACKs to clock the data flow.

ACKs arriving back at the sender arrive at intervals approximately equal to the intervals at which the data packets arrived at the sender [136].

TCP is the protocol used by major Internet applications such as the World Wide Web, email, remote administration and file transfer.

It used on this work to transmit data from home device to specialist station over internet.

3.4 Software Description

3.4.1 General Structure

On the basis of the hardware as described in paragraph 3.2, the integration of the Chronius wearable sensored shirt has needed the implementation of software, which could permit the identification, the transmission and the visualization of the considered signals.

These are definitively:

the three ECG leads

the thorax and abdomen displacement from the inductive bands, and the tidal volume from RespiSENS

the SpO2 and heart rate from the reflectance pulsiximeter

the temperature and humidity measurements

Figure 3.31 represents the general structure of the implemented software, which has been named ShirtSIG System (Shirt SIGnals).

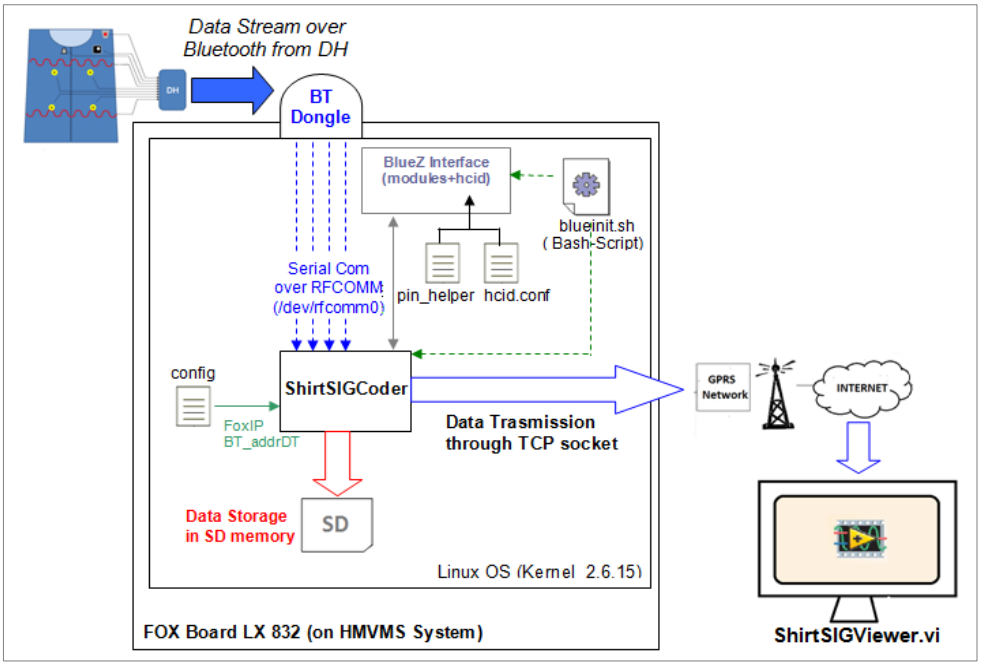


Figure 3.31 - General Structure of ShirtSIG System

The figure shows how several components interact in the general structure, but two in particular may be recognized as main parts:

the ShirtSIGCoder, a C program that runs on the Fox Board Linux environment that

identifies the data frames sent by the Data Handler over Bluetooth RFCOMM serial communication, and transmit them on internet through a TCP socket. It also acts data storage in the SD memory of the Fox Board GPRS kit (see also par 3.2.1).
the ShirtSIGViewer.vi, a LabView interface which allows the visualization of the signals on the remote station of a specialist.
ShirtSIGCoder and ShirtSIGViewer realize the most of the functionalities of the ShirtSIG system, which would run on the same DTS device of the HMVSM.
The way as the whole ShirtSIG system works, and the characteristics and contribution of each component will be better explained in the next paragraphs.

3.4.1.1 BlueZ Interface

BlueZ is the official Official Linux Bluetooth protocol stack.
BlueZ is the official Bluetooth protocol stack for Linux. Its goal is to make an implementation of the Bluetooth wireless standards specifications for Linux.
It was initially developed by Qualcomm, and is available for Linux kernel versions 2.4.6 and up [137]**.**
The BlueZ stack supports all core Bluetooth protocols and layers
Currently BlueZ consists of many separate modules, that are drivers to interface the OS to the low stack level , and utils, that are software and daemons the for the stack managing. (Figure 3.32):
Bluetooth kernel subsystem core
- L2CAP and SCO audio kernel layers
- RFCOMM, BNEP, CMTP and HIDP kernel implementations
- HCI UART, USB, PCMCIA and virtual device drivers
- General Bluetooth and SDP libraries and daemons
- Configuration and testing utilities
- Protocol decoding and analysis tools

-

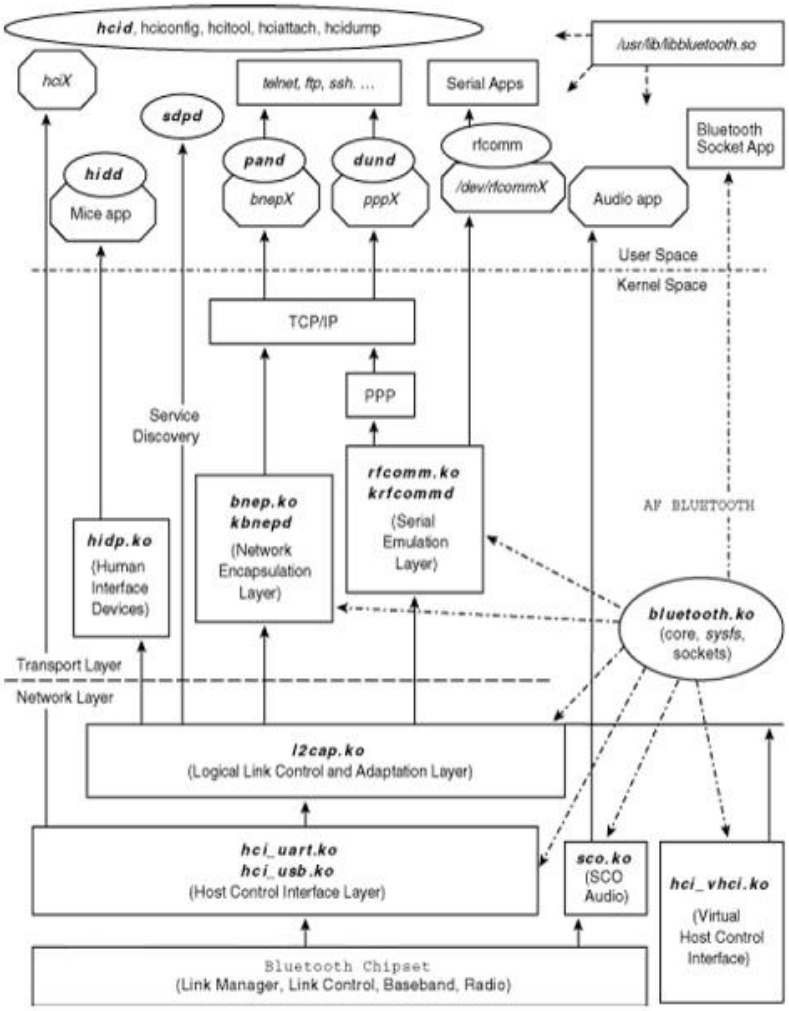


Figure 3.32 - BlueZ stack: modules and utils

For Linux users, BlueZ makes it possible to connect to and thus use Bluetooth devices, such as Bluetooth usb-dongles, mobile phones with Bluetooth, access points and so on. For this reasons, BlueZ has been chosen to be installed on the Linux kernel 2.6.15 of the Fox Board to interface with the USB Bluetooth Dongle (see also 3.2.4).
The installation has been done through the Phrozen SDK 3.0 environment, a dedicated development environment which permits to configure and compile the kernel of the Fox Board Linux OS.

Through the BlueZ modules – bluetooth.ko, l2cap.ko, hci_usb.ko, rfcomm.ko – and the hcid daemon (figure 3.29) has been possible to access to the baseband layers of the Bluetooth connection over the USB dongle, and finally to the RFCOMM serial communication from the Data Handler .
This permits the data stream from DH to be disposable for higher stack level applications, accessing to the device file:

```
/dev/rfcomm0
```

3.4.1.2 Blueinit.sh

Bluinit.sh is a Bourne shell script file contained in the /etc/init.d/boottime folder of the Linux OS file system.
The scripts are text files contain a sequence of instructions.
When a script runs, these instructions are read and executed by the system shell that is the virtual interface between the OS kernel and the user.
Shell scripting offers an true interpreted programming language, allowing to use all the commands of the shell together with common programming constructs (if- then, case, for while).
The language rules depends on the type of shell on which the script running: the Linux kernel OS on Fox Board support the Bourne shell.
The commands in blueinit.sh are listed below (the code is also reported in Appendix A):

```
#!/bin/sh
cdBluez-start
mount /dev/mmc0 /mnt/0 -t vfat -o noatime
mkdir /mnt/0/shirtdata
hcid -f /etc/bluetooth/hcid.conf
/mnt/flash/shirtsigcoder&
```

The scope of the whole script is to initiate the peripherals that interface with ShirtSIGCoder, and to rum the program when the FoxBoard is powered on.
All the script contained in the /etc/init.d/boottime folder, indeed are allowed to be launched at boot time. In particular:
cdBluez-start: initiates the blueZ modules bluetooth.ko, l2cap.ko, hci_usb.ko, rfcomm.ko starting the USB dongle interface.
mount /dev/mmc0 /mnt/0 -t vfat -o noatime makes accessible the SD memory on the file system, mounting it at the /mnt/0 directory with a VFAT (Virtual File Allocation Table)

partition and noatime mount option
mkdir /mnt/0/shirtdata, creates if doesn't exists the main data storage directory on the SD memory card
hcid runs the Bluetooth HCI interface daemon on the basis of the configurations fil e /etc/bluetooth/hcid.conf file. Its structrure is explained below
/mnt/flash/shirtsigcoder& launchs the shirtsigcoder program located in the /mnt/flash directory.

3.4.1.2 hcid.conf and pin_helper file

The file /etc/bluetooth/hcid.conf contains all the options needed by the Bluetooth Host Controller Interface daemon.
It consists of sections and parameters. A section begins with the name of the section followed by optional specifiers and the parameters inside curly brackets (see Appendix A section 1). The valid section names for hcid.conf are:

- *options* contains generic options for hcid and the pairing policy.
- *device* contains lower-level options for the hci devices connected to the computer.

In particular in the options section, a parameter regards the PIN_helper path.
PIN_helper is a file which contains the PIN code trasmitted during pairing process.
The parameter has been set to /etc/bluetooth/pin, that was the PIN_helper position in the file system.
The content of the file was:

0000

that’s simply the same pin code exchanged by the DataHandler.
In the device section, the parameter indicates the local device bluetooth address has been set to the USB Bluetooth dongle address.
With such configuration of the hcid.conf file, a successful pairing procedure can take place between the DataHandler and the USB Bluetooth Dongle. allowing a final correct bluetooth connection between the two devices.

3.4.1.4 ShirtSIGCoder

As mentioned since here, the Fox Board is equipped with a complete Linux operative system.
In such environment also self-made programs are allowed to run.

ShirtSIGcoder is a C program that runs on the DTS FoxBoard, that:

- *connects* to Data Handler device via Bluetooth
- *reads* from the DH data stream through the RFCOMM Serial comunication, accessing to the /dev/rfcomm0 device file
- *recognizes* each dataframe among the DH data Stream
- *extracts* the data core and the timestamp bytes from the dataframe and *saves* them in files on the GPRSKIT SD memory card
- *sends* a compressed version of each dataframe to the Internet opening a TCP session

Figure 3.33 sintetically represents ShirtSIGCoder main concept.

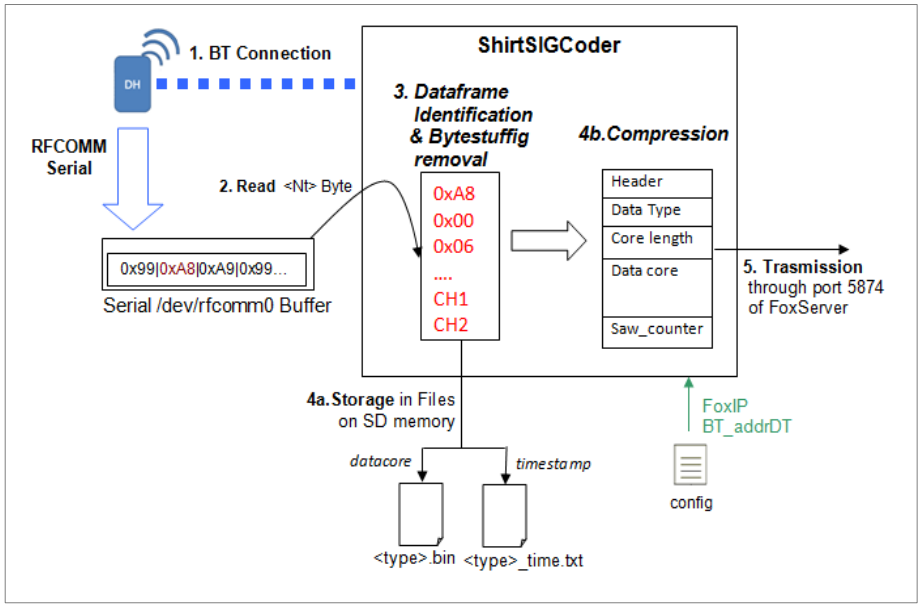


Figure 3.33 - Sintetic view of ShirtSIGCoder main concept

After the Bluetooth connection with the Data Handler has been established, the program reads Nt bytes from the RFCOMM serial communication, accessing to the */dev/rfcomm0* device file: Nt indicates the exact number of bytes disposable on the standard input stream buffer at the the reading time *t*, that is the number of bytes sendt from Data Handler through the Bluetooth connection between two following read operations.
After this, the program proceeds in the identification of each data frame among the read bytes, followed by the bytestuffing removal, the extraction of the datacore and timestamp bytes and thus their storage (see also par 3.3.3) respectively into two type of files in the SD memory.

Bluetooth Connection with the Data Handler

ShirtSIGCoder could realize the Bluetooth connection with the Data Handler thanks to the blueZ interface, initializated by blueinit.sh.
The program tries the connection at start and since it hasn't been established, the tries continues.
When a try goes on success, the connection is established with the Data Handler acting as master device. The pairing process is performed thanks to the hcid daemon and the hcid.conf file configurations.
The device file /dev/rfcomm0 become thus accessible, but the further read operations needs the initialization of the RFCOMM serial communication on the Fox Board side, to make it compatible with the DH data sending.
ShirtSIGCoder does it setting the baud rate ,the parity bit and the stop bit equals to those indicated for the Data Handler (115200 bps of Baud-Rate without any parity, 1 stop bit see also paragraph 3.3.3).
To elicit the Data Handler to transmit data after the connection a start sequence of byte is needed to be sent. That is,

```
0xA8,0x0D,0x00,0x0A,0x0C,0x14,0x09,0x0F,0x00,0x00,0x20,0x17,0x5F
```

and this is transmitted over the initialized RFCOMM serial.
After initialization procedures, the read operation acts as described above.
On running it can happen that the Bluetooth connection falls down: it can be because of several factors such as accidental power off the Data Handler, or movements of the patient over the Bluetooth range field (10 m).
ShirtSIGCoder recognizes this conditions and attempts to restore the Bluetooth connection each time it drops down.
A total of 2000 tries are performed: this represents the threshold beyond which the connection is considered definitively lost.

Frame identification and byte stuffing removal

The frame identification over the read data stream is conceptually based on the data frame start-byte recognition.

When a 0xA8 byte is found among the read sequence, a byte stuffing removal is performed acting on the following bytes the inverse process of the one described in par. 3.3.3.
So when a 0xA9 0x88 or 0xA9 0x89 sequence occurs, it is substitute as follow:

```
0xA9 0x88 → 0xA8
0xA9 0x89 -> 0xA9
```

After byte stuffing removal, the data frame is checked in its structure by the control of the checksum bytes and extracted from the flow for the further operations.

Data storage

The storage files are placed in the main storage directory, created at start-up by the blueinit.sh:

```
/mnt/0/shirtdata
```

and organized for acquisition data and type of signal.
So, that is:

- *data bytes* are saved in **<type>.bin** files, where **<type>** indicates the signal type of the data frame. Thus, we would have *ecg.bin, respisense.bin, pulsi.bin and temp.bin* correspondent respectively to the ecg leads signals, respisense signals, SpO2 and Heart Rate signals from reflectance pulsioxymeter, and temperature and humidity measures.
- *timestamp bytes* are saved in **<type>_time.txt** files where **<type>** indicates the signal type of the data frame. As the data bytes files we would have *ecg_time.txt, respi_time.txt, pulsi_time.txt, temp_time.txt* files

In particular, data bytes are stored in binary format files as raw bytes without any change from the original data frame.
This choice has been made to have an easy and quick way for storage data, and to guarantee a portable format of the storage files.
With a raw binary format indeed, data are soon ready to be successively analysed and elaborated through any commercial analysis software (such as Matlab).
It has been important to provide this feature to ShirtSIG as a telemedicine application, because on this way patient's data can be disposable for further studies over and above they can be visualized in real time.
Queued to each datacore the respective calculated *saw counter* byte is saved.
This is an incremental counter starting from 0 to 256 and then back to 0, used to control the

integrity of the sent data on the client side. It will be better explained on paragraph 3.4.1.5. Timestamp bytes are instead stored in plain text file.
This file contains the timestamp values of the instants when the correspondent data are sampled on the basis of the Data Handler clock. They are in the format:

```
YYYY-MM-DD, HH:mm:SS.MS
```

where YYYY= year, MM=month, DD=day, HH=hour, mm=minutes, SS=seconds MS=milliseconds.
To better manage multiple acquisitions at different times, both data files and timestamp files are automatically located, for each acquisition, in a subdirectory of the main storage directory named as follow:

```
/mnt/0/shirtdata/DDMMYYYYHHmmSSMCR
```

where DD=day, MM=month, YYYY=year, HH=hour, mm=month, SS=second, CS=cents of seconds referred to the time when acquisition starts and R is a random generated number.

Data transmitting

Parallel to the storage process, each data frame is transmitted in a compressed way to the internet through a TCP Session: ShirtSIGCoder in facts acts also as TCP server located at the Fox Board IP address, and a socket is created and posed in listen state on port 5874. When there is a client connection request on the port, data starts to be sent.
To limit the bandwidth consumption over the GPRS, the original data frames are compressed in a smaller package which contains:

- an *header of 4 0xFF bytes*, used for synchronization
- the *data type byte*
- the *length in bytes* of the data core
- the *data core bytes*
- the *saw counter*

The config file

ShirtSIGCoder interacts at start-up with the *config file.*
The config file is a text file, used in common with the HMVMS software, contains the initialization parameters of the system.

The config file furnishes to ShirtSIGCoder the Data Handler Bluetooth Address and the actual Fox Board IP address.
The first is used to open the Bluetooth connection with the DH, the second needs to start the TCP server and open the socket.
The use the config file allows the ShirtSIG System to be used in different networks and with different Data Handler devices in an easy way.
The control parameters indeed, can be modified only changing a text file.

ShirtSIGCoder source code and complete flow chart

ShirtSIGCoder in written in C programming language and compiled through the gcc-cris compiler, an embedded C compiler for the Fox Board architecture provided by the Phrozen SDK environment.
The complete source code package is composed by the main file *shirtsigcoder.c* and by several libraries implements the modules for the functionalities of the program.
In particular:

- *seriale.c, seriale.h* contain variables, headers and functions for the serial interface
- *framefunc.h, framefunc.c* contain variables, headers and functions for the data stream management, the bytestuffing removal, the data storage and the data frame compression
- *blueconns.h, blueconns.c* contains variables, headers and functions to manage the Bluetooth connection
- *gprskit.h, gprskit.c* contain variables, headers and functions to start the TCP server, open the sockets and send data over TCP
- *addons.c, addons.h* contain headers and functions to interface with the *config file*

All the source code files mentioned here are reported in Appendix A.
In the next pages Figure 3.34 shows the complete flow chart of ShirtSIGCoder.

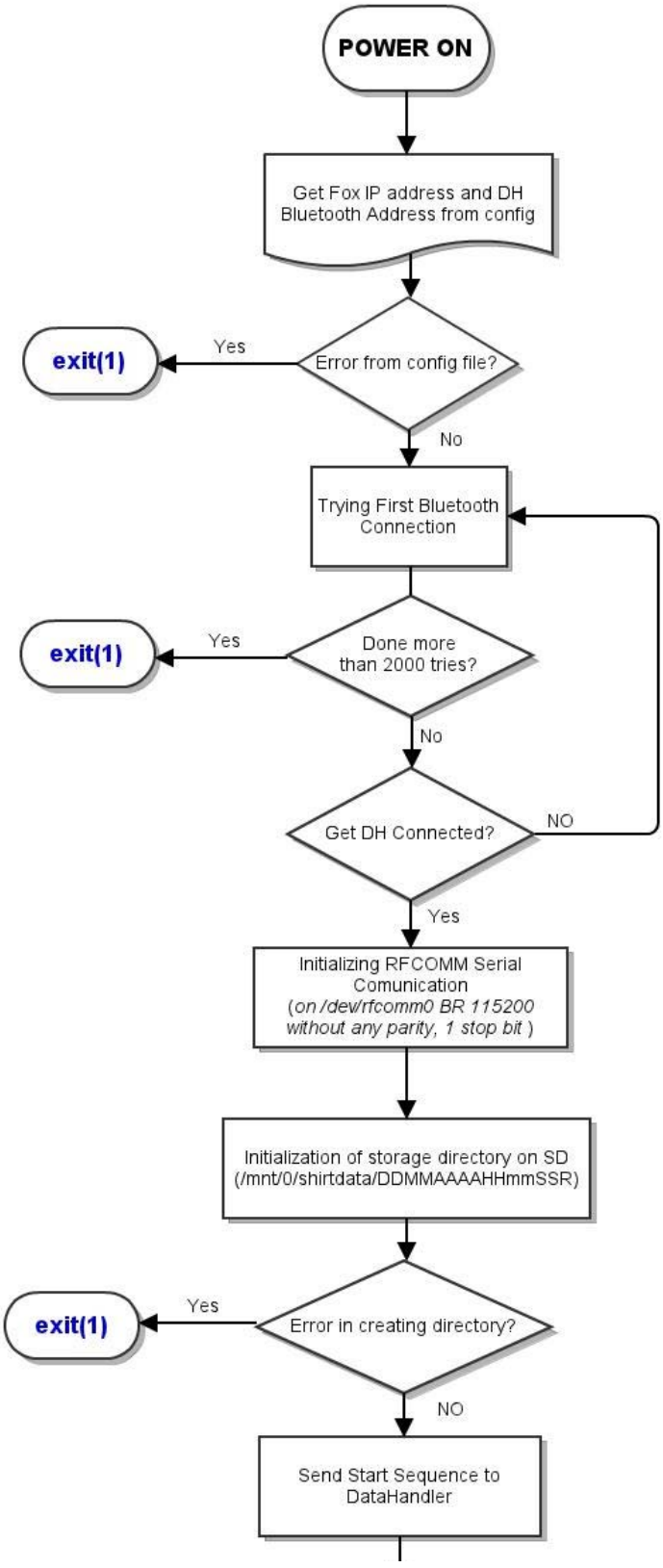


Figure 3.34 -1 ShirtSIGCoder flow chart Initialization procedures

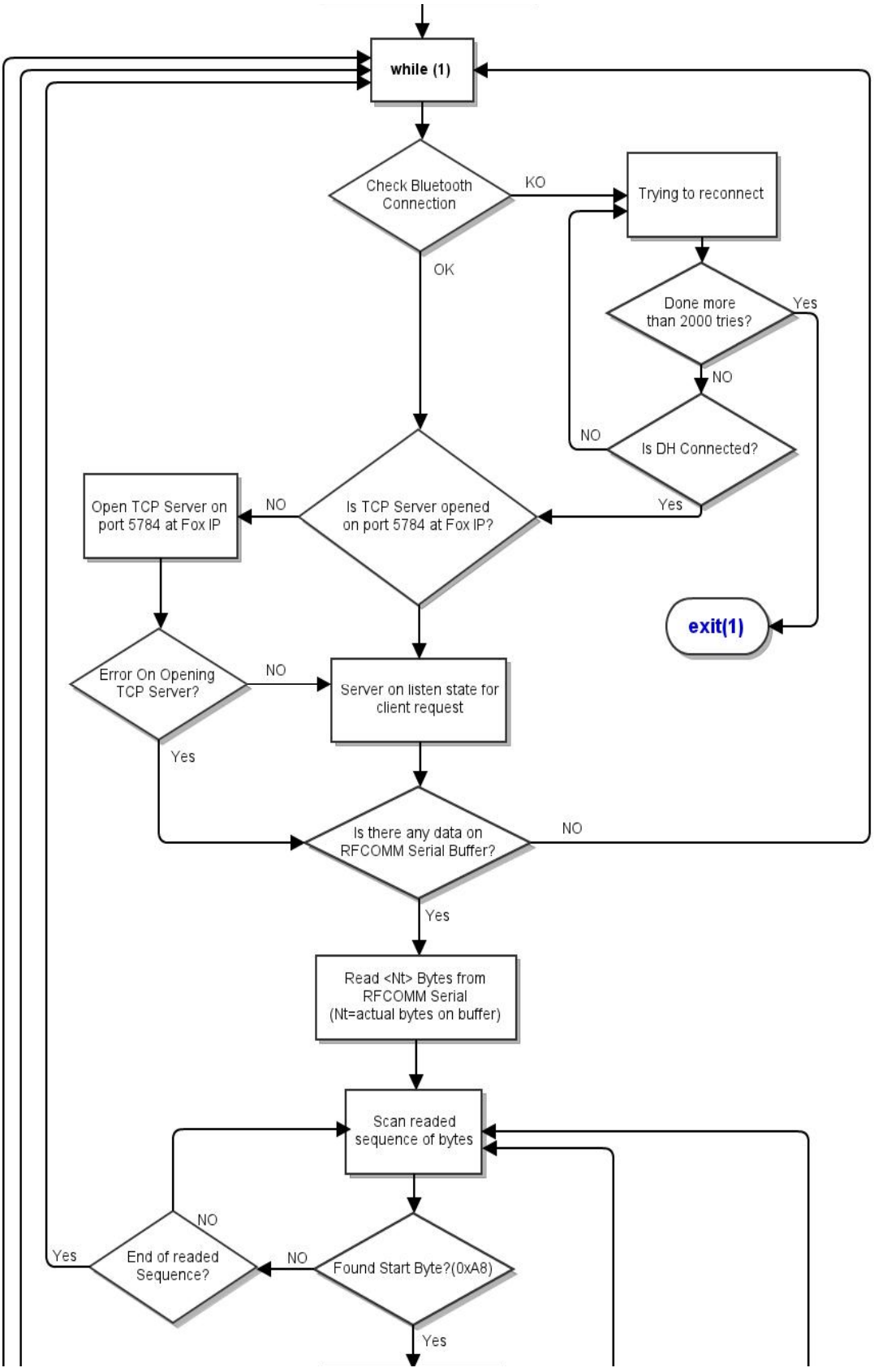


Figure 3.34-2 - ShirtSIGCoder flow chart: Main while loop, Read operations and data frame identification

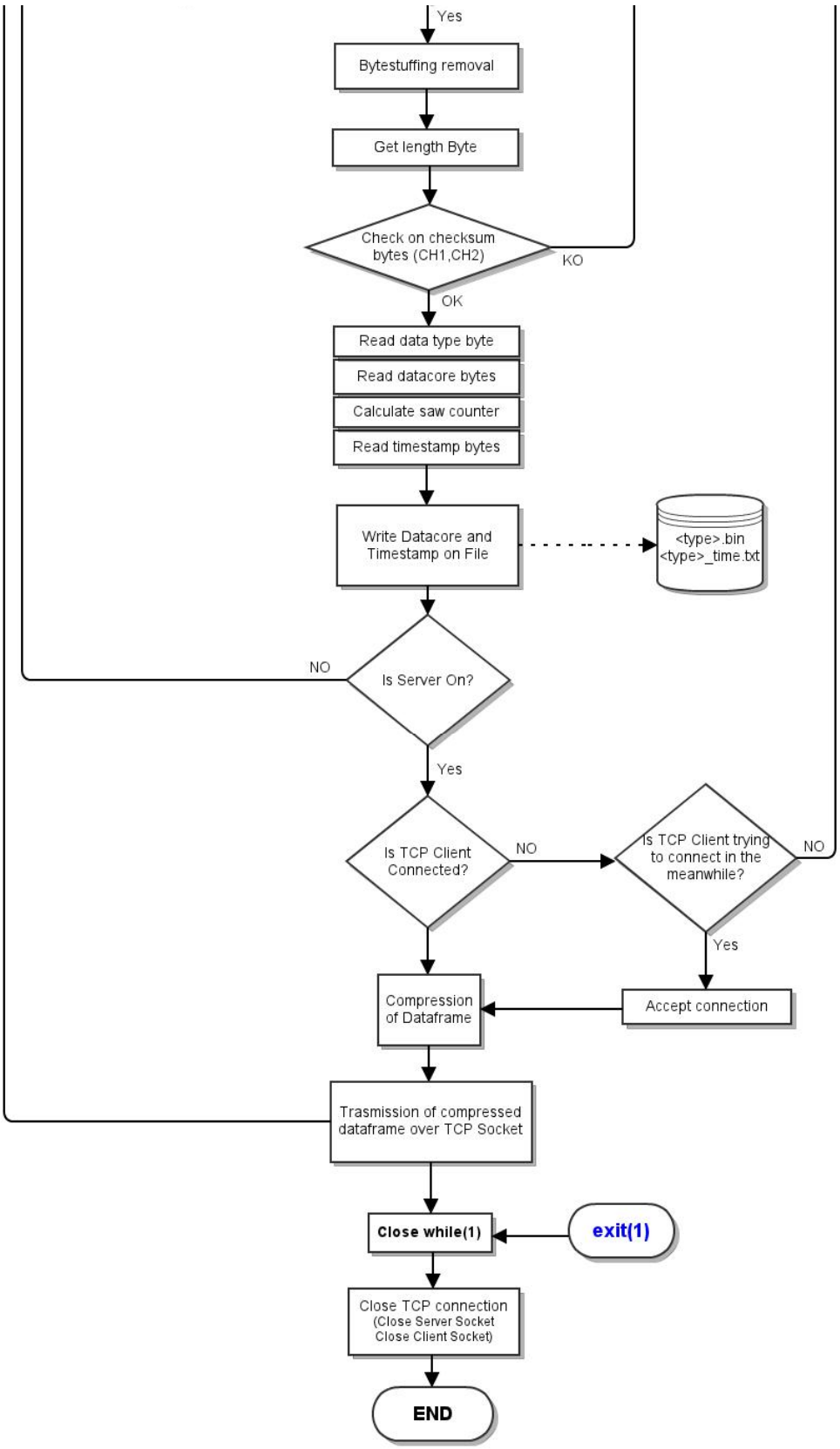


Figure 3.34 - 3 - ShirtSIGCoder flow chart: Main while loop, bytestuffing removal, data storage and transmission, end of the programThe program starts getting the Fox IP address and the Data Handler Bluetooth address from config file.

If the operation goes on success, the initialization procedures occur first with the initial Bluetooth connection attempt, and the with initializations of the storage directories and the server.
After the start sequence has been transmitted the main while loop begins.
Into the while loop are performed the functions implement the main functionalities of ShirtSIGCoder (read from RFCOMM serial buffer, data frame recognition and bytestuffing, data storage, compression and transmission).
At each loop the Bluetooth connection and the TCP client connection are checked, and if they are dropped down, the program will rise them up again.
The label exit(1) in the flow chart means a critical end of the program.
It occurs when the program can't have the possibility to perform the next operations and a forced stop is mandatory.
The exit(1) procedure is summoned by:
an error in getting parameters from config file
more than 2000 tries in the Bluetooth connection attempts.
an error in creating storage directory.

3.4.1.5 ShirtSIGViewer.vi

ShirtSIGViewer.vi is a LabView application for the real time visualization of the patient's signals coming from the Chronious Wearable Shirt.

It acts as TCP client application accessing to port 5874 at the Fox Board IP address, and receiving the data sent by ShirtSIGCoder.

ShirtSIGViewer.vi is implemented to be easily installed on the specialist computer.

It offers an easy and intuitive interface for the remote monitoring of the patient's state.

Figure 3.35 displays a screen shot the front panel of ShirtSIGViewer.vi on running that finally is the user interface.

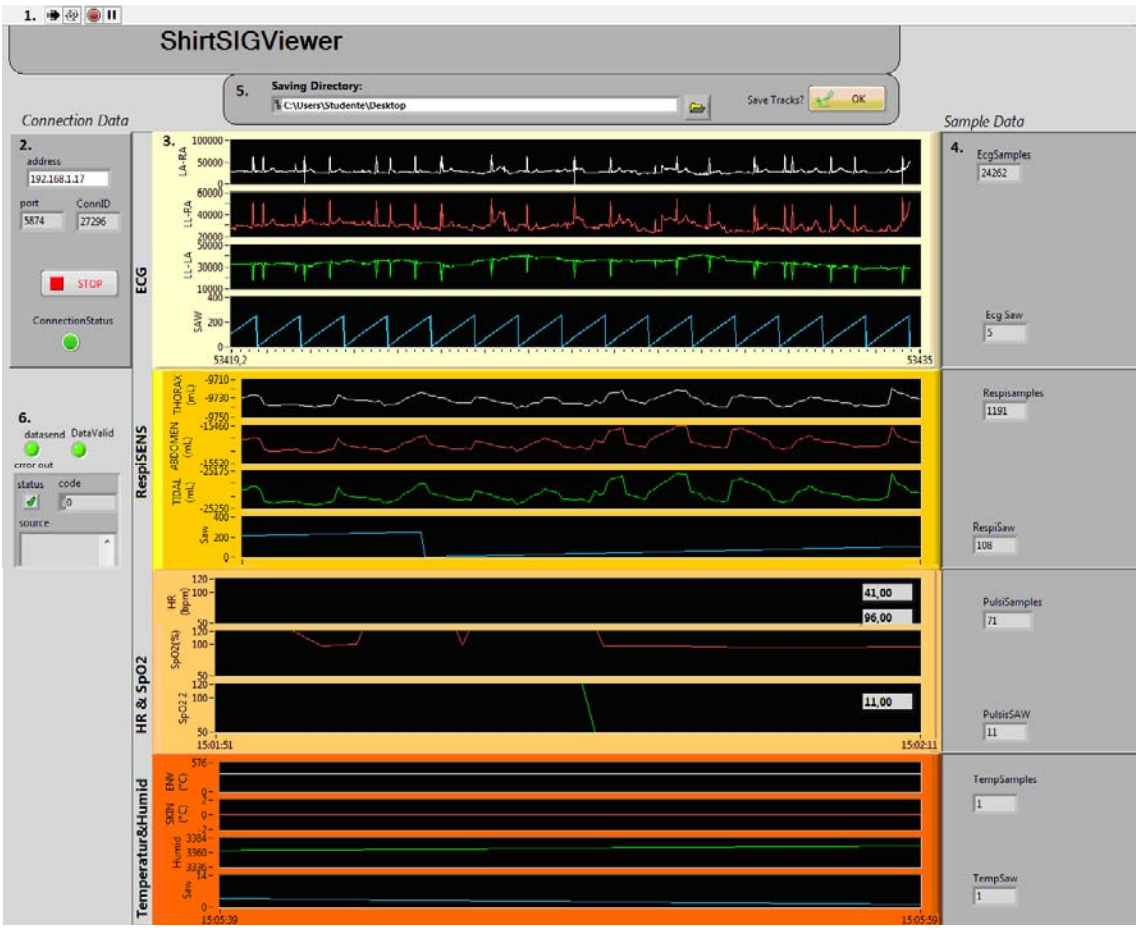


Figure 3.35 - ShirtSIGViewer.vi front panel

As the figure shows, several modules can be identified:

the *Start and stop buttons* on the Labview control bar

- *the Connection panel:* it contains the socket parameters (IP address and port) where the clients would connect, the connection ID number, a connection status led that

turns on when the connection is established and a 'Stop' button that can be pushed to interrupt the TCP session.

- *the signals tracks,* organized by the signal type. There are the three ECG leads (in order LA-RA, LL-RA,LL-LA) in the lite pink case, the RespiSENS signals (Thorax, Abdomen and tidal volume) in yellow case, the SpO2 and HR signals in the salmon pink case and the temperature and humidity measures in the orange case. Every set of signals has in the lower part the saw signal that is the graphical representation of the saw counter of the correspondent sent data. The saw signal and the saw counter are used for the instantaneous check of a data-lost event or of any irregularity in the data transmission. As explained in the previous paragraph the saw counter is a progressive number from 0 to 256 assigned to each compressed data frame. When a data is lost during transmission, the progression interrupts and this reflects in an instantaneous change of the shape of the saw signal.
- *the counters panel*, for each type of signal contains the number of samples received and the numeric value of the saw counter.
- *the save options panel,* ShirtSIGViewer permits to save the visualized tracks also on local files. The save options panel allows to the path of the saving directory and contains the button to start the data saving on file.
- *the error panel* , contains two led indicators respectively for the presence data over the TCP connection (DataSent) and they validity as compressed data frame (DataValid) and the indicator for the error values.

The complete block diagram that stays beyond of ShirtSIGViewer.vi front panel is reported in Appendix B**.**

It can be divided in 3 main functional blocks.

The first block is constituted by the *connection starter*, a while loop that contains the function to open the client socket and to connect to server socket on the chosen IP and port: the while loop continues until the TCP session is started. Then the ID of the connection established is returned to the following blocks.

The connection starter block corresponds to the connection panel on the front panel.

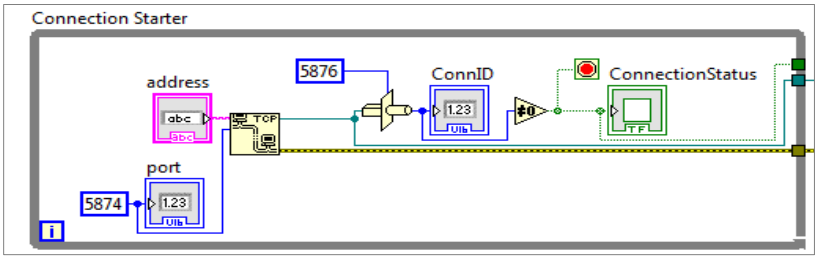


Figure 3.36 - Connection Starter block

The second block, *Data reading and checking* starts with the main while loop of the application.

The block receives the connection ID from the connections waiter, and reads the compressed data frames over the TCP transmission buffer in a string format (Figure 3.37 A).

The data read are thus converted in numeric array of byte for the following elaborations (Figure 3.37 B): the control of the presence of data over TCP connection (DataSent) is here performed.

After the numeric array conversion, data are checked to be a valid compressed data frame (DataValid): the control is performed comparing the length of numeric array of data read with the minimum threshold for a valid compressed data frame (Figure 3.37 C).

In conclusion Figure 3.37 D shows the saving parameters which appear on the saving option panels.

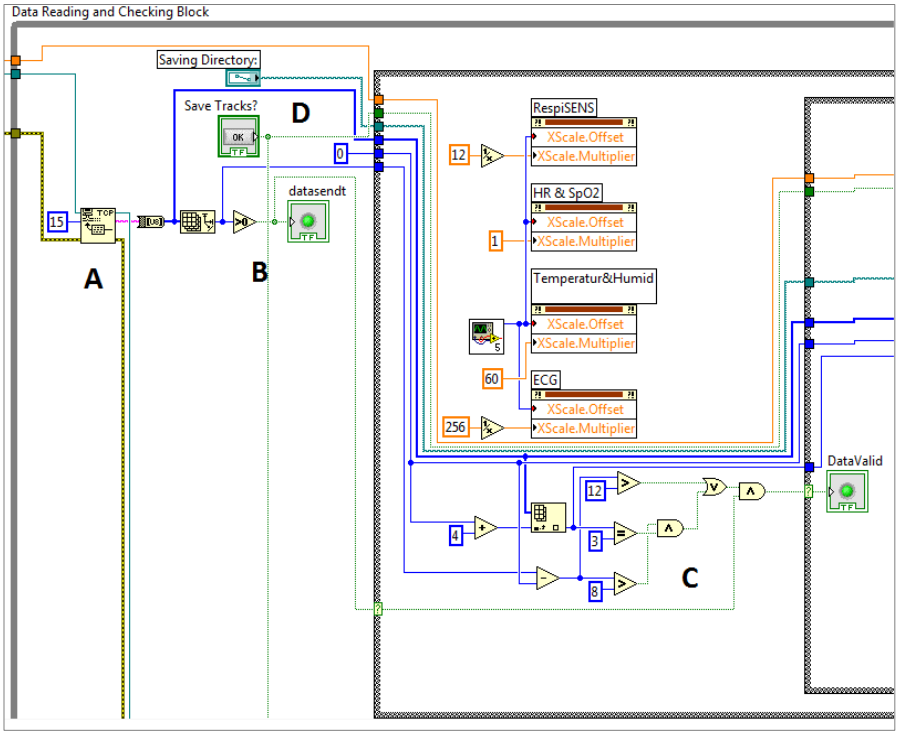


Figure 3.37 - Data Reading and Checking block

The last functional block realizes the visualization of the tracks and the data saving if this option is checked. First of all data frames are converted from single bytes to significant integer values of the particular signal: for example in the case of the ECG type, the MSB and LSB of each lead within the data frame are combined to have the complete numeric value of the signal (Figure 3.38 A). The same operation is done for the other signal types. Then data run on two parallel circuits, one for the track visualization (Figure 3.38 B) and one for saving on file if this feature is activated (Figure 3.38 C).

The data are saved in text files stored in the select directory.

The files are named as follow:

TypeDDMMYYYYHHmmSS.txt

where type=type of the signal (ECG, Respi, Pulsi, TempHumid) and DD=day, MM=month, YYYY=year, HH=hour, mm=month, SS=second referred to the time the save starts.

Each file is organized in columns separated by a tab character: the columns contain the numeric values of the signals and the correspondent saw counter on the same row.

For example for the ECG.txt file the first number is the saw counter of the data frame. The last three numbers of a row are the values of three ECG lead in the same order they are visualized (LA-RA, LL-RA, LL-LA).

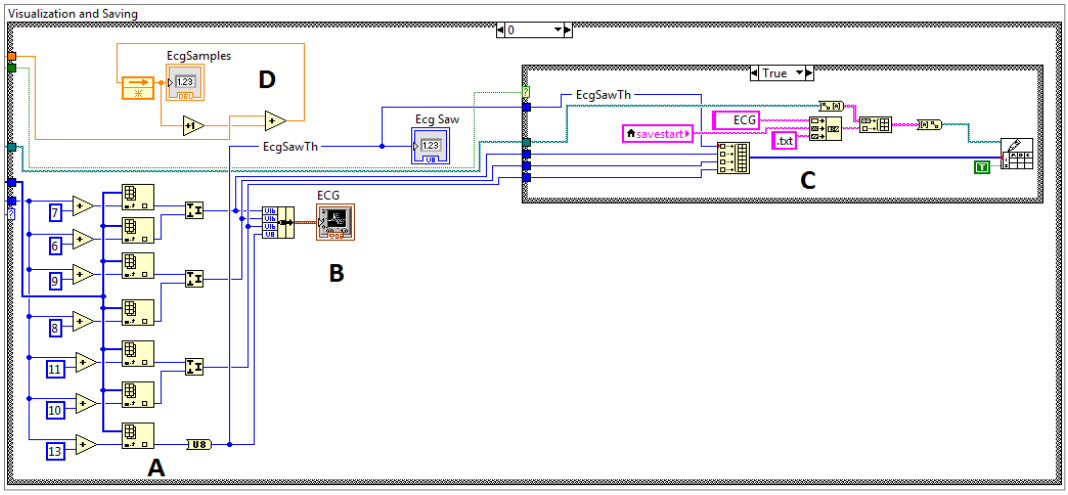


Figure 3.38 - Visualization and saving block

Figure 3.38 D represents the sample counter implementation.

The visualization and saving block is adapted for each signal type: a case selector performs which version of the block has to run on the basis of the data type byte within the data frame.

The block diagram ends with the function stops the TCP connection and the error handler: the first runs outside the main while loop when the 'Stop' button on the connection panel is pushed. The second manages and visualizes on the error panel the errors the errors that rises up on the VI(Figure 3.39).

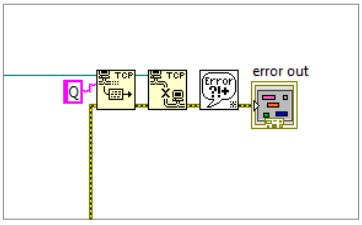


Figure 3.39 - TCP Connection Closer and Error Handler

3.4.1.5 Resumptive overview of the ShirtSIGSystem

Figure 3.40 offers a schematic resume of the data flow in the ShirtSIGSystem.

The signals measured by the sensor on the Chronious Shirt are digitalized and sent over a Wireless Bluetooth connection in the form of data frames according to the transmission protocol described in par 3.3.3. The ones considered in this work are the ECG signals; the RIP signals the HR and SpO2 signals from a reflectance pulseoximeter, and the temperature and humidity measures from the Solianis sensor. Each data frame contains the timestamp of the sampling instant and a code of the signal type together with other additional information. The ShirtSIGCoder on the DTS reads and identifies the data frames from the RFCOMM serial communication stream over Bluetooth connection between the Data Handler and the DTS through an USB Bluetooth dongle: the data frames are then decoded, compressed and sent through a TCP connection on the Internet.

The data core and the timestamp information within the data frames are extracted and stored in files on the SD memory installed in the FoxGM of the GPRSKIT plugged to the Fox Board LX 832, the core unit the DTS. The signals from the shirt can be remotely visualized by ShirtSIGViewer a LabView application, which connects as TCP client to the DTS and receives the compressed data frames. The signals are graphically represented as continuous tracks on the visualization panels of the ShirtSIGViewer user interface.

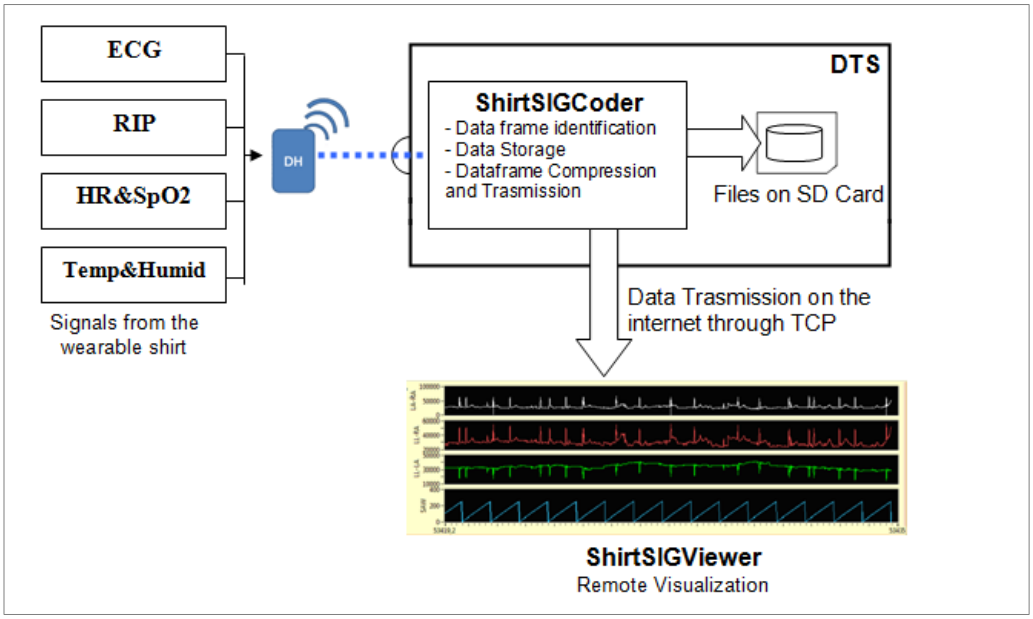


Figure 3.40 - Resumptive Overview of the ShirtSIG System

Chapter 4 - Simulations, tests and Results

The firmware developed as described in the previous chapter has been tested in order to evaluate its capabilities and performances.The tests and the simulations has been focused on the application of the Chronious Wearable System in combination with the DTS, where two software are running, the one for acquiring ventilator's signals (HMVMS) and the one for wearable system signals acquisition (ShirtSIG System).

The main goals, that have guided the tests, were:

- to verify the performances and the reliability of the functionalities implemented on the whole system.
- to observe how the information brought by signals gathered from the shirt could integrate the ones from the ventilator, offering to the clinician a more complete real-time monitoring tool of the patient state with the final aim of the performance of a more responsive and accurate remote titration.

The test session, has been divided in three main phases :

Bench tests phase; the general functionalities of the system such as data frame recognition data storage performances, reliability of data transmission and real time response have been analyzed in normal working conditions and together with the HMVSM in order to understand the system behaviour.

Reliability test on long time; the system has been tested to be active for long time simulating the working in the night hours.

Pathological events recognition test; the application of the system together with the HMVMS has been observed on a healthy subject performing the simulation of several clinical conditions concerning the chronic respiratory diseases. These tests have been done to characterize the clinical use of the system and its effectiveness for the home monitoring and remote titration in chronic respiratory care.

4.1 Bench test phase

The bench test phase has been done to monitor the main functionalities implemented into the ShirtSIG system.
The aim was to understand the system behaviour in normal working conditions, together with the HMVSM.
In particular the focus was on data frame recognition, data storage, data transmission and real time response in order to verify the ability of the system to handle the signals provided by the Chronious Wearable System without loss of information.

4.1.1 Experimental Setup and Methods

The integrity of the data at each stage of the manipulation performed by ShirtSIG software – from data reading from RFCOMM serial stream, to data sending through TCP protocol over the net - has been analyzed.
It has been evaluated by verifying the visual correspondence of the signal shapes among the different stages and counting the number of data frames recognized for each signal type directly at RFCOMM serial buffer output, on the files for data storage by ShirtSIGCoder and finally received by the Labview program ShirtSIGViewer.
The test has been consisted in the performance of acquisitions from the shirt wore by a healthy subject aged 27 breathing through a nasal mask connected to a Bipap mechanical ventilator (BIPAP® SYNCHRONY®, PHILIPS Respironics, Pittsburgh, Pennsilvenia, USA).
Three different sets of acquisitions have been performed in order to test the system in different running conditions:

1) *ShirtSIGCoder runs on the DTS, HMVMS not running and ShirtSIGViewer client not connected*; in this situation it's possible to evaluate data frame recognition over Bluetooth RFCOMM serial data stream and data storage performances. Figure 4.1 shows a schematic view of the experimental setup used for this running condition and the points (R, S) where the data frames have been counted; respectively at read (R) and at storage (S).

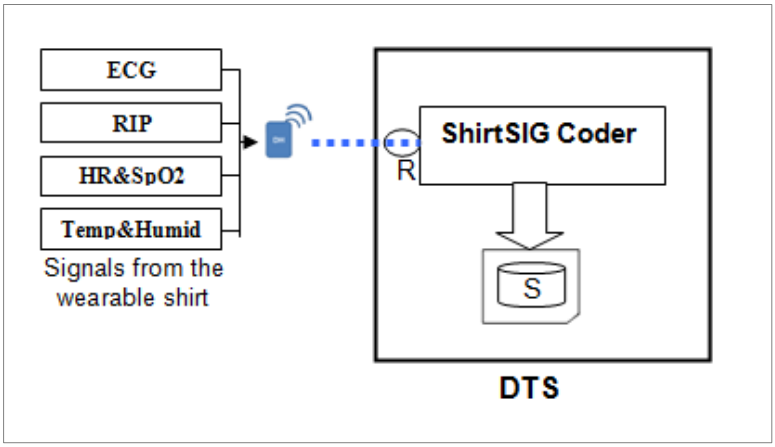


Figure 4.1 - Schema of the experimental setup in running condition 1: ShirtSIGCoder runs on the DTS, HMVMS not running and ShirtSIGViewer client not connected. R, S are the data frame count points, R=at read, S=at storage

2) ShirtSIGCoder runs on the DTS, HMVMS not running, ShirtSIGViewer client connected; in this configuration it is possible to evaluate the data transmission performances and the global performances of ShirtSIGSystem running alone. Figure 4.2 shows a schematic view of the experimental setup used in this running condition and of the points (R,S,T) where the data frame has been counted; respectively at read (R) and at storage (S) and at transmission (T).

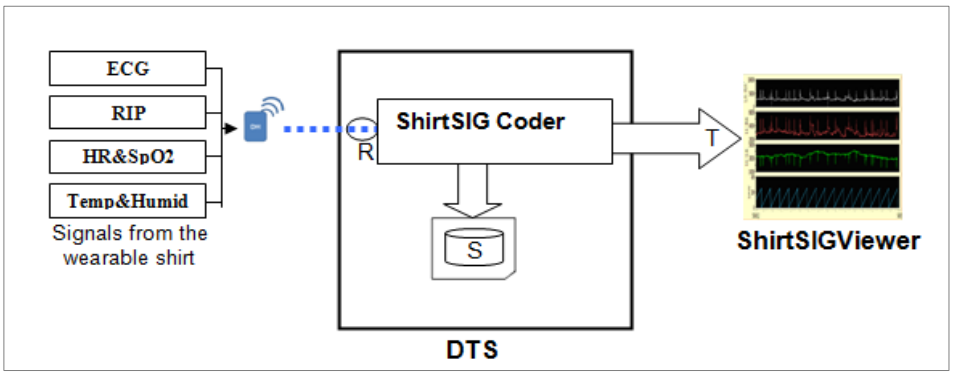


Figure 4.2 - Schema of the experimental setup in running condition 2: ShirtSIGCoder runs on the DTS, HMVMS not running, ShirtSIGViewer client connected. R,S,T are the data frame count points, R=at read, S=at storage,T=at transmission

3) ShirtSIGCoder runs on the DTS with HMVMS running and ShirtSIGViewer client connected; in this configuration it is possible to evaluate ShirtSIGSystem global

performances together with the HMVMS. Figure 4.3 shows a schematic view of the experimental setup used in this running condition and of the points (R, S, and T) where the data frame has been counted; respectively at read (R), at storage (S) and at transmission (T).

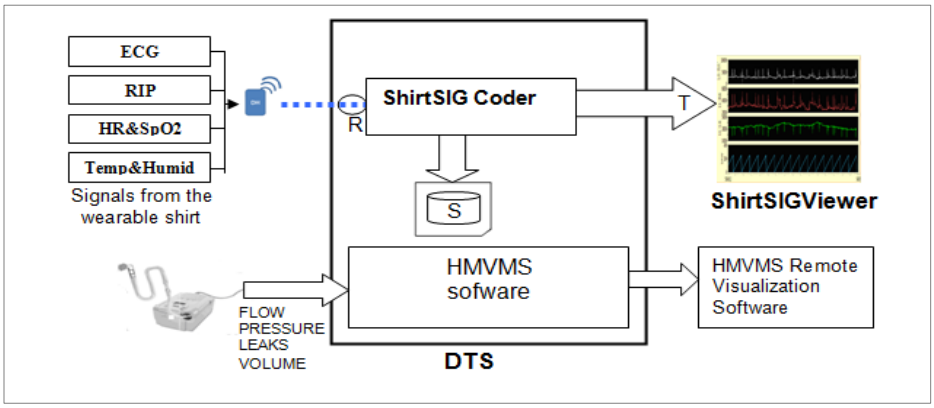


Figure 4.3 - Schema of the experimental setup in running condition 3: ShirtSIGCoder runs on the DTS with HMVMS running and ShirtSIGViewer client connected.R,S,T are the data frame count points, R=at read, S=at storage, T=at transmission

The HMVMS acquired signals (flow, pressure, leaks, volume) from the ventilator connected to the DTS through an USB plug: the signals from the ventilator were sent on the internet and visualized by remote visualization software on an external laptop.

Each test set in each different running condition comprised 5 acquisitions sessions each one lasts three minutes.

For conditions 2) and 3) has been observed also the real time responsiveness of simulated events like coughs, apnoeas and asynchronies on the transmitted signals.

The analysis of the signal shapes and the determination of the number of data frames storage and transmitted e of the elaboration chain, as previously described was done with the help of a Matlab software.

The Matlab software scanned the raw data files obtained directly from the RFCOMM serial communication and counted the amount of data frames of each signal recognized on the stream. The software then compared the counted data with the amount of frames stored in the files on the SD Memory and with the amount of data received by ShirtSIGViewer.

Contemporarily, the data frames counted from the raw data files and from the stored files on SD Memory were graphically visualized as signal tracks and compared in their shape to verify their correspondence.

Finally the software calculated the S/R, T/S and T/R percentages where R=n°data frames recognized at reading, S=n° stored data frames, T=n° transmitted data frames.
A comparison with the theoretical amount of data frames that would be expected to be received by the Bluetooth communication was also done: the expected amount of data frame for each signal type has been calculated considering the acquisition time and the data transmission frequencies, as follow:

$$Nex = T * ft \qquad [4.1]$$

where Nex=expected amount of data frame, T=time of acquisition, ft=data transmission frequency. The evaluation of Nex values for each data type contributed to final the calculation of the S/Nex percentage ratios.
The analysis described has been performed for each repetition of the fives in a set, and for all the running condition considered.
The average values of S/R, T/S, S/Nex percentages referring to the particular running conditions setup, have been finally computed for each data type.
Taking on example the average value of the S/T for the ECG signal in running condition 1, it has been obtained as mean value of the S/T percentages calculated for the ECG signal in each of the five acquisitions of the set as follow:

$$(SR)_{ECG-M} = \frac{\sum_{i=1}^{5} (SR)_{ECG-i}}{5} \qquad [4.2]$$

where S/R_{ECG-M} represents the mean value e S/R_{ECG-i} the percentage value referred to the single acquisition.

4.1.2 Results

The results of the numerical analysis described above is reported in Table 4.1

A. Running condition 1

.

Signal Type	S/R	S/Nex
	%	%
ECG	100,0	69,1
RESPI	99,7	69,7
PULSI	100,0	69,8
TEMP	100,0	75,0

B. Running condition 2

Signal Type	S/R	T/S	S/Nex
	%	%	%
ECG	100,0	100,0	62,0
RESPI	100,0	99,4	62,3
PULSI	100,0	98,6	63,7
TEMP	91,7	90,0	55,6

C Running condition 3

Signal Type	S/R	T/S	S/Nex
	%	%	%
ECG	100,0	100,0	18,2
RESPI	100,0	99,4	18,9
PULSI	96,8	97,6	18,7
TEMP	0,0	90,0	0,0

Table 4.1: Average values of the S/R, T/S and S/Nex ratios in running conditions 1 (A) 2(B) 3(C) for each signal type.

Table 4.1 shows the average values of S/R, T/S and S/Nex ratios for each signal type in each running condition considered.

The obtained results show how in all the three running condition, the data can be considered correctly recognized, storage and transmitted by the ShirtSIG System after the reading operations. The S/R, T/S mean values are nearest the 100% in about all the analysis conducted. During the elaboration chain the data integrity can be considered maintained.

Observing the S/Nex values instead, appears that this percentage ratio became lower in the running conditions 2 and 3 rather than in the running condition 1 (Figure 4.4).

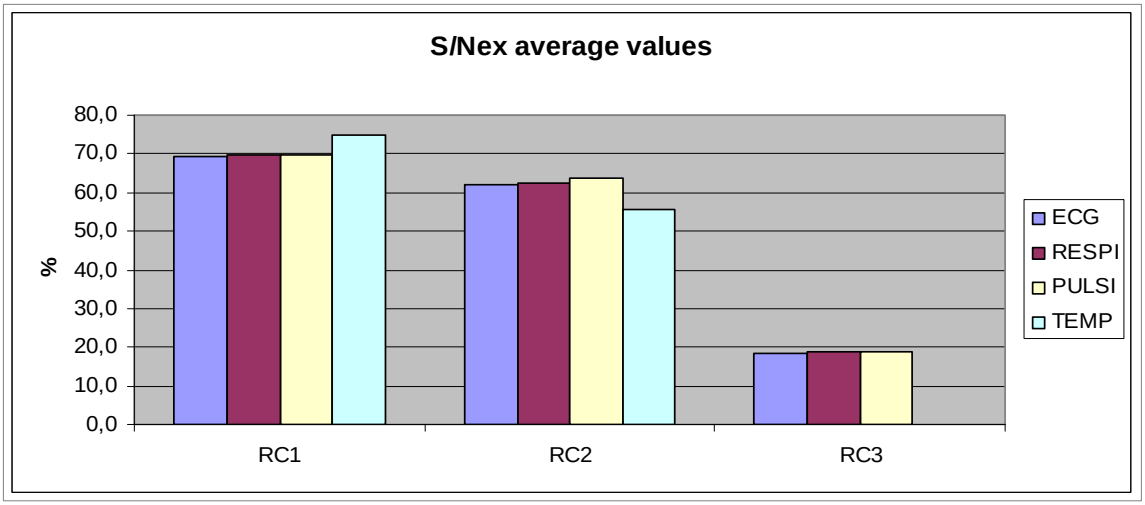


Figure 4.4 - S/Nex average values for each signal type in running condition 1 (RC1), running condition 2(RC2), running condition 3(RC2)

This means that even if the data elaboration chain works identifying, storing and transmitting all the frames read as previously observed, the total amount of read packages over the RFCOMM serial buffer became lower in running conditions 2 and 3.

In the case of the ShirtSIG System running together with the HMVSM this percentage is about at 50% for each signal type. The increased computational load for the Fox board processor lead also to a strongly visible delay in the visualization of the transmitted signals on the ShirtSIGViewer in such running conditions.

The real time responsiveness of the simulated events (cough, asynchronies, apnoeas) evaluated by the visualization delay, is high in the running conditions 2. (Without HMVMS installed) and is really low – that means that a great visualization delay occurs – in running condition 3 (with HMVMS installed).

4.1.3 Additional tests excluding ECG signal storage and transmission

Tests on two additional running conditions has been done after the results obtained by the first tests. These further running conditions exclude the storage and transmission of the ECG signal data frame: this choice has been done to reduce the computational load.

The ECG signal in fact is the one with the highest sampling frequency (256Hz), thus meaning that a lot of processing resources are used by ShirtSIGCoder: this implies an high number of operation done by the processor in a second, that represents a substantial contribute to the computational load.

4.1.3.1 Experimental Setup and Methods

As the firsts, the additional bench tests has been conducted acquiring signals from a healthy subject aged 27 who wore the shirt and breaths through a nasal mask connected to a Bipap mechanical ventilator (BIPAP® SYNCHRONY®, PHILIPS Respironics, Pittsburgh, Pennsylvania, USA).

The two additional running conditions considered have been:

4) ShirtSIGCoder runs on the DTS, HMVMS not running, with ShirtSIGViewer client connected excluding ECG data frames storage and transmission. Figure 4.5 shows a schematic view of the experimental setup used in this running condition and of the points (R, S, and T) where the data frame has been counted respectively at read (R) and at storage (S) and at transmission (T).

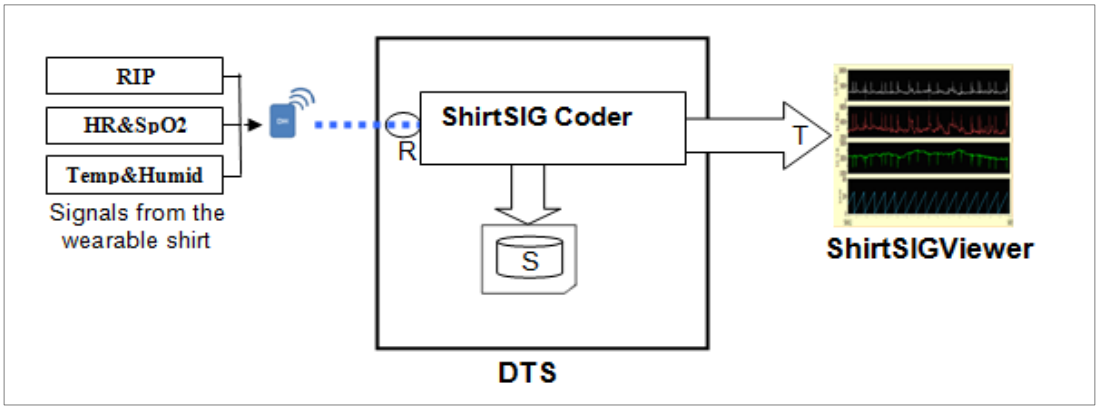


Figure 4.5 - Schema of the experimental setup in running condition 4: ShirtSIGCoder runs on the DTS, HMVMS not running, with ShirtSIGViewer client connected excluding ECG data frames storage and transmission.R,S,T are the data frame count points, R=at read, S=at storage, T=at transmission

5) ShirtSIGCoder runs on the DTS with HMVMS running and ShirtSIGViewer client connected excluding ECG data frames storage and transmission. Figure 4.6 shows a schematic view of the data flow in this running condition and the points (R, S, and T) where the data frame has been counted; respectively at read (R), at storage (S) and at transmission (T).

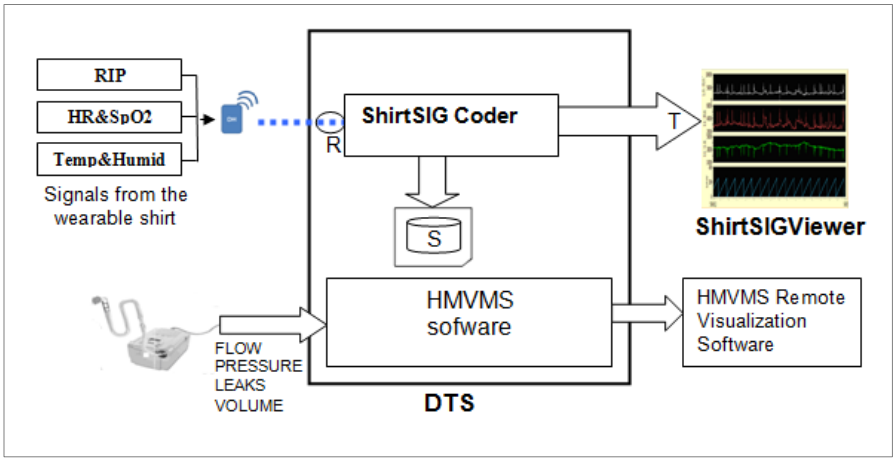


Figure 4.6 - Schema of the experimental setup in running condition 5: ShirtSIGCoder runs on the DTS with HMVMS running and ShirtSIGViewer client connected excluding ECG data frames storage and transmission. R, S, T are the data frame count points, R=at read, S=at storage, T=at transmission

As in running condition 3, the HMVMS acquired signals from the ventilator connected to the DTS through an USB plug: the signals from the ventilator were sent on the internet and visualized by remote visualization software on an external laptop.

4.1.3.2 Results

The average values of S/R, T/S and S/Nex percentages in the added running conditions are reported in Table 4.2, divided by signal type.

D. Running condition 4

Signal Type	S/R	T/S	S/Nex
	%	%	%
RESPI	96,8	99,0	62,3
PULSI	99,3	99,3	63,7
TEMP	100,0	73,3	50,9

E: Running condition 5

Signal Type	S/R	T/S	S/Nex
	%	%	%
RESPI	99,5	99,7	46,5
PULSI	100,6	98,5	45,6
TEMP	100,0	25,0	50,0

Table 4.2: Average values of the S/R, T/S and S/Nex ratios in running conditions 4(D) and 5(E) foreach signal type

Analysing the obtained results, in can be observed that the S/Nex values are higher in comparison with the corresponded ones reporter in tables 4.1.B and 4.1.C.

Figure 4.7 graphically shows the comparison between the S/Nex values in running conditions 2, 3 and 4, 5.

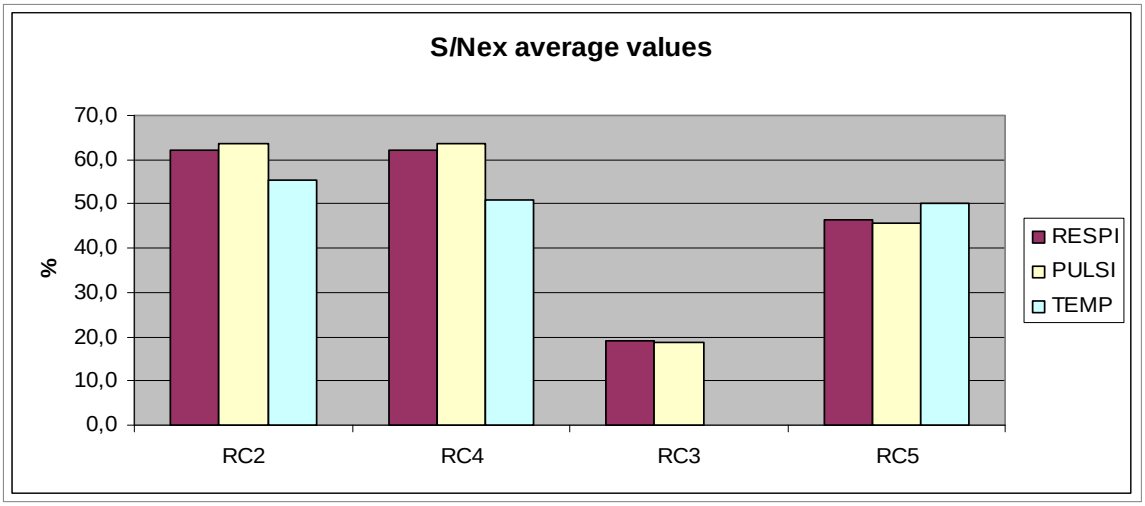


Figure 4.7 - S/Nex average values for each signal type in running condition 2 (RC2), running condition (RC4), running condition 3(RC2), running condition (RC5)

4.2 Reliability test of long time acquisition

In order to evaluate the usability of the ShirtSIGSystem for long periods of acquisitions, such as during a night session, a reliability test of long time acquisition has been performed.

The test wanted to check the reliability of the software running for all night time of hours: the aim of the test was to control the behaviour of system during the period, using a log file where all the events occurring during the acquisition period were reported.

The ability of the ShirtSIGCoder to reconnect to Data Handler after a connection drop down was also observed.

4.2.1 Experimental Setup and Methods

The ShirtSIG System was tested on a healthy subject wearing the shirt for 4 nights during sleep. Figure 4.8 resumes schematically the experimental setup of the test.

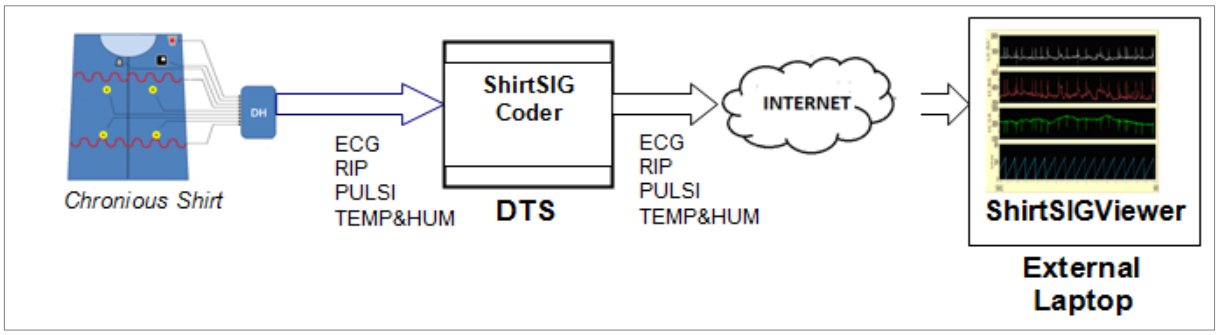


Figure 4.8 -Schema of the experimental setup of the reliability test on long time acquisitions

During the night hours, the ShirtSIGCoder was running on DTS reading, storing and transmitting the signals from the shirt and ShirtSIGViewer visualized them on an external laptop connected to the Internet.

The test was considered successful if after the fixed end of the acquisition, the system could continue to work in all its functionalities and no critical conditions leading to crash happened.

4.2.2 Results

On the 4 acquisitions performed:

3 times the system worked properly sending and saving incoming data, and reported no

crashes neither problems.
1 time the system crashed and stopped to receive signals because a problem of Bluetooth connection between the Data Handler and the DTS occurs.

4.3 Pathological events recognition test

A test on a healthy subject has been conducted in order to test the ability of the system to show some pathological events typical of sleep disordered breathing patients.
This test wanted to observe the usefulness of the ShirtSIG for the remote recognition of some events in combination with the use of the HMVMS.
The aim was to analyse how the signal from the subject by the shirt could provide significant additional information to the clinician, that can help him to titrate at distance in a timely way and more fitted to the patient breath dynamics.
Such an aim has been perceived performing the acquisition test on a healthy subject performing a simulation protocol studied to reproduce the most common breathing events related to chronic respiratory diseases during night time.

4.3.1 Experimental setup and Methods

The test has been conducted on a male subject aged 27 who wore the Chronious wearable platform and sustained a CPAP ventilation of 4 cmH2O through a nasal mask, generated by a PHILIPS Respironics BIPAP® SYNCHRONY® home mechanical ventilator.
Figure 4.9 shows the schematic view of the experimental setup used for the test.

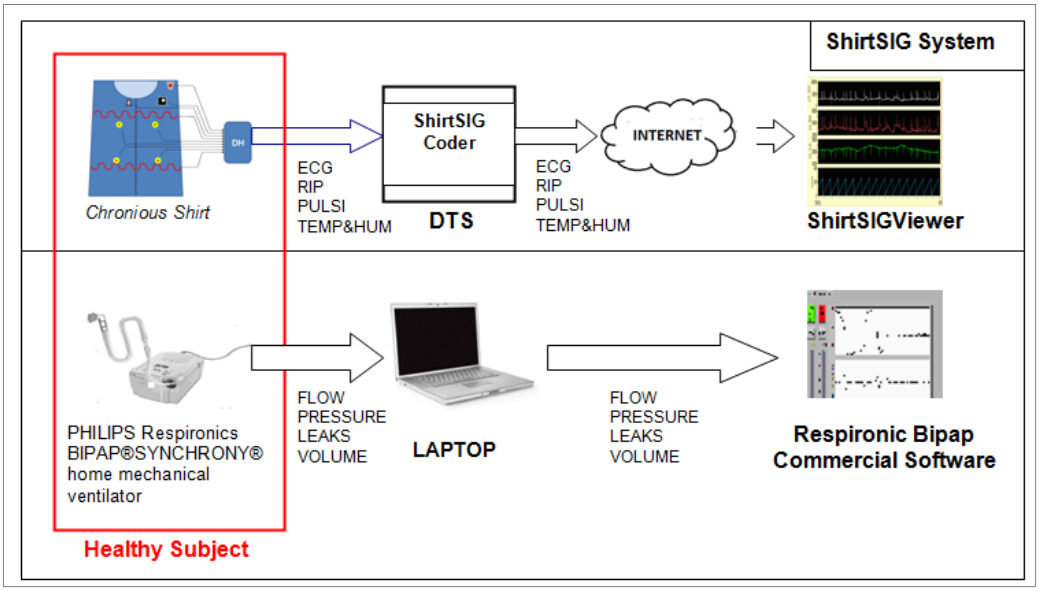


Figure 4.9 -Experimental setup of the pathological events recognition test

During the test the ShirtSIGCoder was active on DTS, the ShirtSIGViewer connected and running on an external laptop.

Considering the results of the bench test, the HMVMS was avoided to be installed on the DTS to release computational load and to permit the ShirtSIGCoder to run in the best conditions.

The signals from the ventilator have been acquired by commercial software installed on the external laptop: the ventilator was connected to the laptop through an USB serial adapter to the laptop.

The software acquired the same signals acquired by the HMVMS software that are for the remote titration: they are air flow, pressure, volume and leaks from the nasal mask (this last is a useful indicator for the mask fitting).

The subject undergone the test, performed a protocol of simulation of the most common pathological breathing disorders concerning the chronic respiratory diseases.

The protocol consisted in 3 acquisitions of 10 minutes each, structured as a set of periods of normal breathing followed by the occurrence of a simulated respiratory abnormality.

In the first 10 minutes, the clinical conditions of the affection by obstructive sleep apnoeas syndrome have been simulated.

The period of acquisition was so articulated:

- *1 Total Lung Capacity* manoeuvre for synchronization

- *4 minutes* of quite breathing
- *30 seconds* of breathing muscles efforts with glottis-closed and upper airways excluded - - from the air flow to simulate the obstructive apnoea conditions
- *other 4 minutes* of normal breathing performance
- *other 30 second* of breathing with glottis-closed and upper airways excluded from the air flow to simulate the obstructive apnoea conditions
- *1 minute* of quite breathing

In the second 10 minutes, a simulation of central sleep apnoeas was acted as follow

- *1 Total Lung Capacity* manoeuvre for synchronization
- *4 minutes* of quite breathing
- *30 second* of breath holding with forced block of the movements of the chest wall - and the abdominal region, to simulate central sleep apnoea
- *other 4 minutes* of normal breathing performance
- *other 30 second* of breath holding with forced block of the movements of the chest wall and the abdominal region, to simulate central sleep apnoea.
- *1 minute* of quite breathing

The last 10 minutes has provided the simulation of the chest wall-abdomen asynchronies, typical of COPD affection:

1 Total Lung Capacity manoeuvre for synchronization

4 minutes of normal breathing performance

30 second of chest-wall abdomen asynchronies simulation, contracting the abdominal muscles and the diaphragm during inspiration

other 4 minutes of normal breathing performance

other 30 second of chest-wall abdomen asynchronies simulation

1 minute of quite breathing.

Figure 4.9 resumes the complete protocol structure:

	0-4’00’’	4’00’’-4’30’’	4’30’’-8’30’’	8’30’’- 9’00’’	9’00’’–10’00’
First 10 min	Quite breathing	OSAS simulation	Quite breathing	OSAS simulation	Quite breathing
Second 10 min	Quite breathing	Central Sleep Apnoeas sim.	Quite breathing	Central Sleep Apnoeas sim.	Quite breathing
third 10 min	Quite breathing	C-A asynchronies. sim.	Quite breathing	C-A asynchronies sim.	Quite breathing

Figure 4.10- Simulation protocol structure (C-A asynchrony = chest wall-abdomen asynchronies)

4.3.2 Results

The evaluation of the significance and the usefulness of the real time information added by the signal acquired by the ShirtSIG System to the global patient remote monitoring, has been done with a visual analysis of those signals versus the one acquired from the ventilator during the same test periods.

The next pages report a static representation of some extracts from the tracks acquired from the shirt and from the ventilator, both recorded in the same particular periods of the execution of the simulation protocol.

Figure 4.11 shows the recorded tracks during a normal breathing period.

Figure 4.12, Figure 4.13 and Figure 4.14 are instead related respectively to an OSAS simulation time, a central apnoeas simulation time and a chest wall-abdomen asynchronies simulation time.

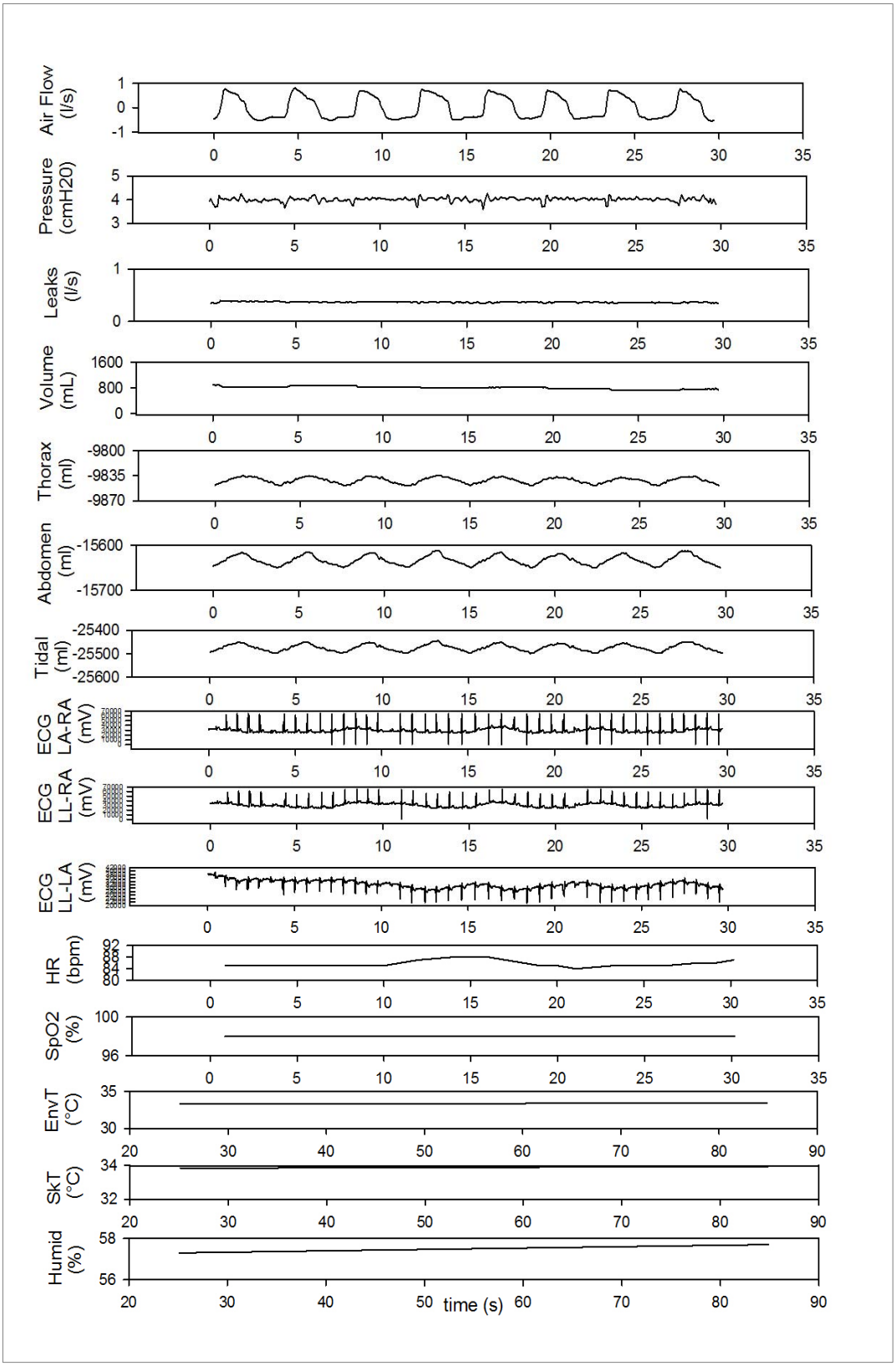


Figure 4.11 - Quite breathing tracks

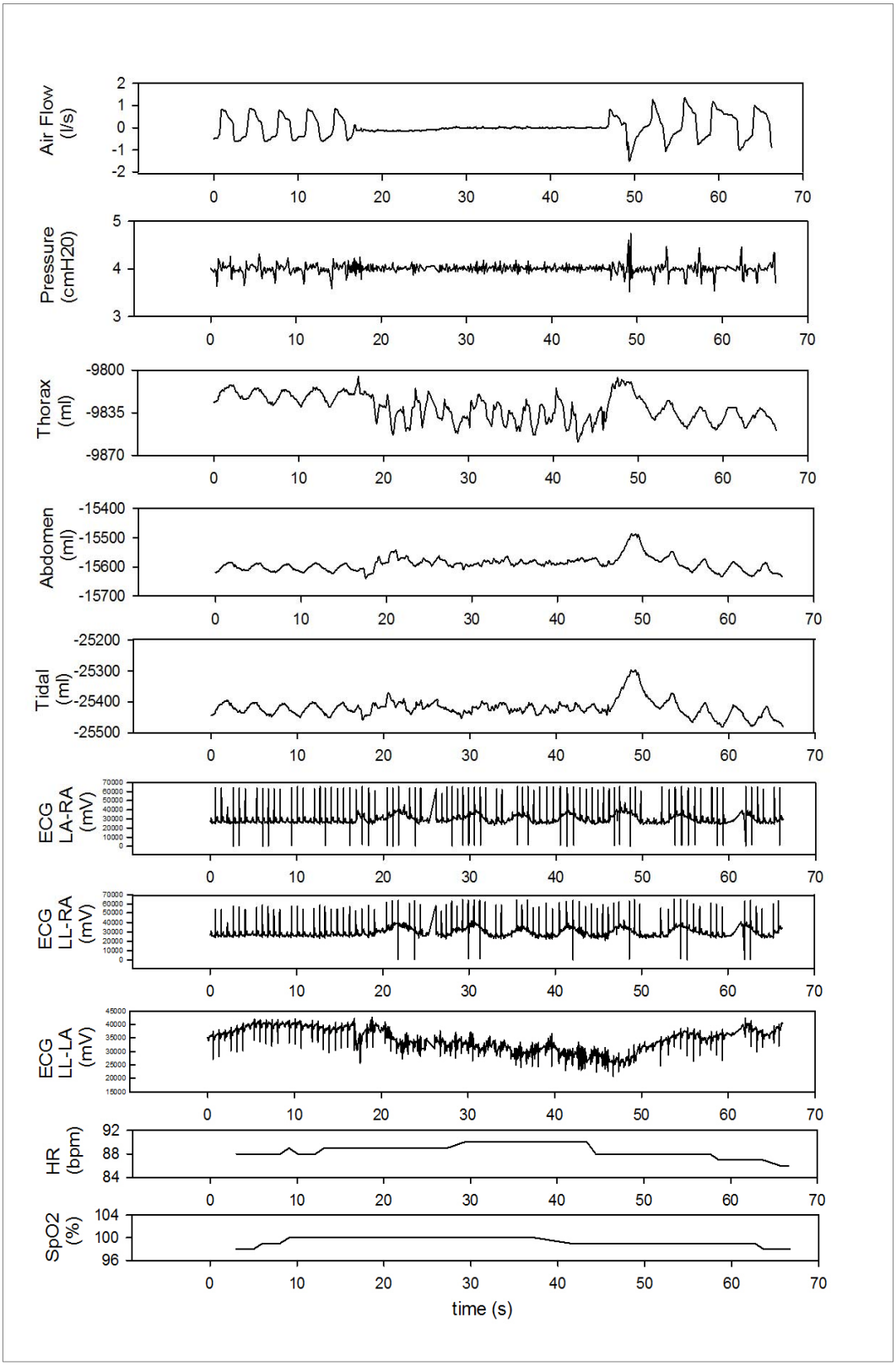


Figure 4.12 - OSAS simulation tracks (For a better visualization there have been reported only the tracks useful for events recognition)

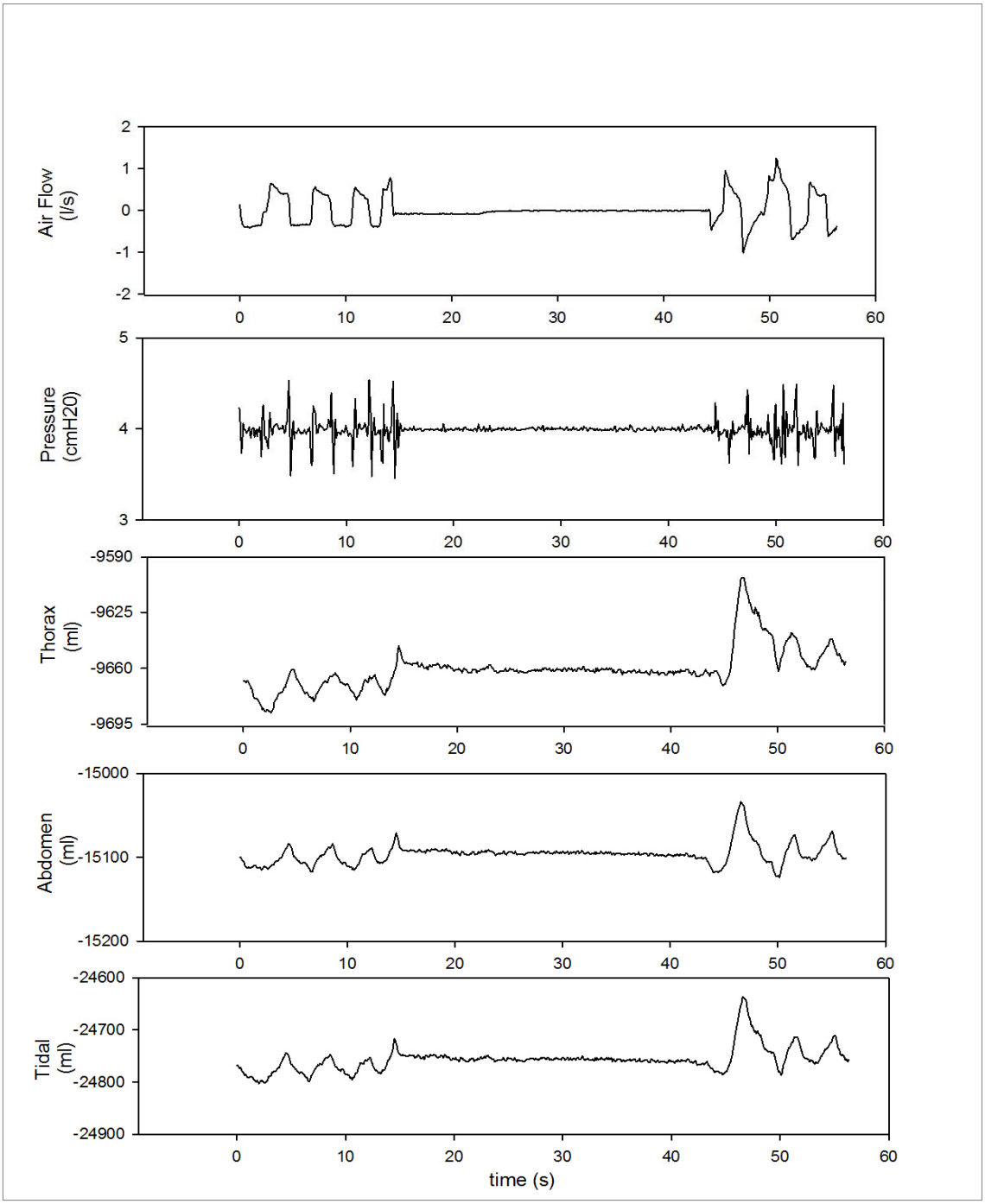


Figure 4.13 - Central Apnoeas simulation tracks (For a better visualization there have been reported only the tracks useful for events recognition)

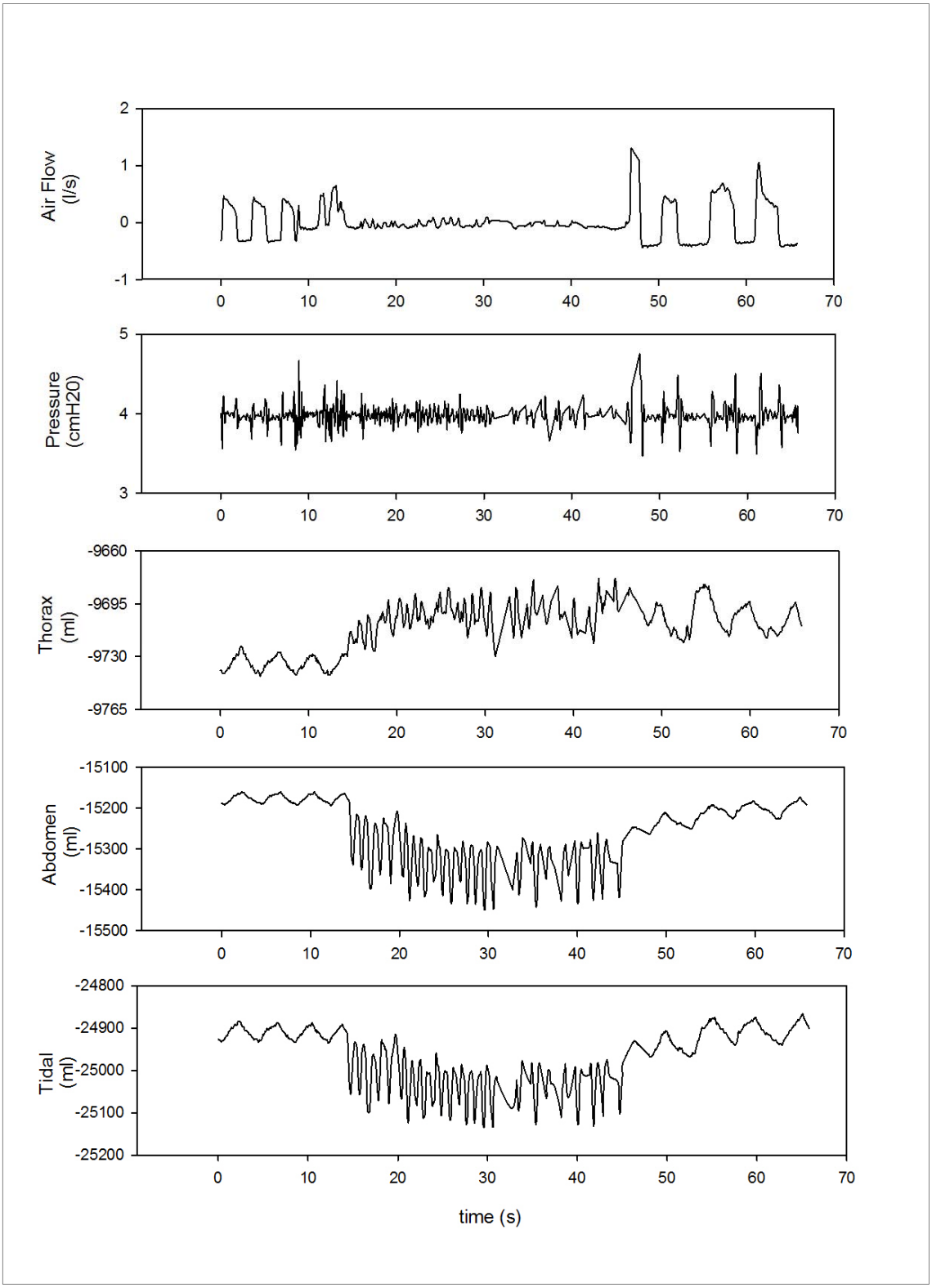


Figure 4.14 - Chest-wall Asynchronies simulation tracks (For a better visualization there have been reported only the tracks useful for events recognition)

By the comparison from the shirt and the ventilator static tracks in the same particular time and among the different times considered, several consideration can be done that are useful to characterize the use of the ShirtSIG system during the remote titration.
To have a clearer framework of them, the consideration are here reported divided by the particular simulation test they refer to.

Normal breathing

During normal breathing the flow and the pressure signals from the ventilator and the RIP of the wearable system signals are in phase, synchronized to the breathing rhythm.
The ventilator's data bring information about the dynamics of the air at the entrance of upper airways; the wearable system's are instead related to the mechanics of the respiratory system and to the movements done by the thorax and abdomen in the breath acts.
During inspirations the air flow provided by the ventilator increases to reach a peak and the pressure of the air measured marks negative values because a depression occurs within the mask: these phenomena are associated to a synchronized increase in volume of both thorax and abdomen that are recorded as positive displacements by the RIP since a maximum is reached at the end of inspiration. The same dynamic of the thorax and abdomen signals, is obviously reflected on the tidal volume.
The expirations occur after the peaks, with a decrease of the flow accompanied by an increase in the measured pressure due to the air put out in the mask from the mouth.
The thorax and the abdomen reduce their volume and a negative displacement is measured since a minimum is reached at the end of expiration.
It is possible to see the same dynamic is on the tidal volume signal, which is the sum of abdomen and thorax signals of the shirt, and the global dynamics described since here denote the physiological patterns of the flow, pressure and RIP signals.
Observing the ECG signal, the R-R distance does not vary significatively and thus the heart rate is roughly constant
The SpO2 is on a physiological saturation value of about 98%

Obstructive apnoea simulation

The main consequence that figures out from a first observation of the tracks is that during the time the apnoeas persist, the flow volume and pressure tracks flat to zero.
This is an indicator of the obstruction of the upper airways, simulated in the test by the

glottis closure.
Even if the air passage through the upper airways is not accomplished, the thorax and the abdomen continue to move in a synchronous way, to attempt the breath start: the RIP tracks even if with an increasing breathing rhythm, follows breathing dynamic composed by an inspiration and an expiration time similar to the physiological one.
The breath rate increases in response to the lack of oxygen and thus to the desaturation: the SpO2 recorded values decrements in response to the decrease of the dissolved oxygen in blood, and this phenomenon is particularly evident at the end of the apnoea period.
The heart rate increases following the breath rate.

Central Sleep Apnoeas simulation

Observing the central apnoeas simulation tracks, it is particularly notable that the RIP signals flatten to zero as the ventilator signals during the apnoea period.
This is a distinctive indicator of a central classified sleep apnoea, which differentiates it from an obstructive sleep apnoea.
Normally such phenomenon is caused by the interruption of the nervous control on the respiratory muscles (see also Chapter 1) which leads to their immobilization.
During the simulation it has been reflected on the RIP signals with no displacements recorded at the thorax as at the abdomen level and a zero tidal volume results.

Chest wall-Abdomen Asynchronies simulation

As described in par 1.4.1.2 the chest-wall asynchronies occur frequently in COPD patients as a consequence of the structural changes in mechanical properties of the lungs caused by inflammation and emphysema.
Chest-wall asynchronies can be highlighted by the RIP signals as shown in Figure 4.14.
During the simulation performance, the thorax and abdomen displacements are clearly in counter phase from second 15 to second 45.
The Chest-wall asynchronies influences also the ventilator signals: the lack of synchronicity between the thorax and abdomen causes a general flow reduction (which in pathological conditions worsen the flow reduction caused by obstructions related to COPD) and a modification of the normal respiratory pattern. The flow and pressure signals assume a discontinuous abnormal pattern.

Chapter 5 - Conclusions and future developments

5.1 Conclusions

The aim of this work of thesis was to merge together two complementary systems in order to perform a real time home patient monitoring and to test the feasibility of such a system during nocturnal noninvasive mechanical ventilation in order to be applied for the treatment of sleep disordered breathing on COPD patients.

The proposed system is composed of the Chronious wearable system - an ergonomic designed shirt equipped by several physiological sensors, that allows to control continuously patients' physiological parameters - and the Data Transmission Server (DTS) , a telemonitoring system developed at TBM Lab which allows the real time monitoring of a sleeping patient breathing through a mechanical ventilator at home, directly from the hospital, acquiring different ventilation parameters, of pressure and flow, leaks, and allows the physician to tailor the administered ventilation at distance, choosing the best values for each the single patient.

These features are provided only connecting via internet to the DTS, a remote station based on a Fox Board LX 832 multipurpose embedded device located at patient's home, capable to be connected to any commercial ventilator and to access to the Internet through GPRS connection.

The integration of the two systems was aimed to create a telemedicine system able to provide physicians a tool for the remote titration of the home mechanical ventilation in a real time and personalized way. COPD patients that need a more accurate and difficult titration can be monitored at distance by several sensors and parameters that help the physician to better titrate and follow patient's home mechanical ventilation.

In particular some specific signals have been considered to be monitored from the shirt: a 3-leads electrocardiogram, the volume displacements of thorax and abdomen from two RIP bands, the measures of heart rate and hemoglobin saturation from a reflectance

pulseoxymeter and finally the environmental and body temperature and the air humidity measures from a set of dedicated sensors.

The ShirtSIG System has been implemented to get these signals from the shirt over a Bluetooth connection with the Data Handler - a microcontroller-based acquisition system plugged to the t-shirt that can realize Bluetooth class 2.0 connections- thanks to the ShirtSIG Coder, C software that runs on the DTS.

The ShirtSIG system was in fact projected to act together with the HMVMS in order to constitute the global telemedicine system described above.

ShirtSIGCoder reads the data frames of the signal sent by the Data Handler on the RFCOMM serial stream realized over the Bluetooth connection, storages the data read and transmits them on the Internet through a TCP connection.

The signals transmitted can be remotely visualized by the ShirtSIG Viewer, a Labview software installed on the specialist station.

After its implementation, the ShirtSIG system has been evaluated in its general performances and reliability.

A bench test and a reliability test on long time, has been then conducted.

The bench test checked the system in the main functionalities of ShirtSIGCoder analysing data storage performances, reliability of data transmission and real time response, in several running conditions that gradually increase the computational load sustained by the Fox Board on the DTS

Three running conditions have been primarily taken in exam, activating progressively the functionalities of the system: in the first condition only data storage has been set on, in the second condition data transmission was added and finally in the third one ShitSIGCoder run with all the functionalities active concomitant to the HMVMS system installed - software+ventilator connected through USB- and running on the same the DTS.

A set of 5 acquisitions lasted 3 minutes each one has been performed for each running condition. The integrity of the data along the elaboration chain has been evaluated counting the number of data frame received for each signal at each stage of elaboration (R=n°read, S=n°stored, T=n°transmitted) for every repetition.

On the basis of the values obtained, the S/R, T/S, and S/Nex percentages and their average values on the five acquisition for each running condition and for each data type were calculated (where Nex= n° of data frame expected in the acquisition time according to the

correspondent sampling frequency) to understand the extent of eventual data loss or corruption in all the acquisitions conducted.

Starting from the results described in the previous chapter it can be inferred that in the running conditions examined- that constitute the main probable conditions persist in the possible applications of the system - data frames can be considered correctly stored and transmitted by the ShirtSIGCoder since they are read from the RFCOMM Bluetooth serial stream.

Observing the S/Nex average values, they appear in a decreasing trend from the first to the third running condition: by this observation it can be hypothesized that the increasing computational load for the Fox Board processor due to the greater number of activities performed from conditions 1 (only storage) to condition 2 (storage and transmission) continuing on condition 3 (ShirtSIGCoder runs together the HMVMS) influences the ability of ShirtSIGCoder to read from the serial buffer in a fast and timely way, resulting in few data frames disposable to be subsequently decoded in the same time.

In the case of the ShirtSIG System running together with the HMVSM the S/Nex average value is about at 50% for each signal type.

The increased computational load for the Fox board processor lead also to a strongly visible delay in the visualization of the transmitted signals on the ShirtSIGViewer in such running conditions.

The results of the additional tests conducted considering two further running conditions effort the assumption that an high computational load can compromise the reading operation from the RFCOMM serial stream by ShirtSIGCoder: the two additional running conditions considered replicate the second and third running conditions previously explained but differ from them by the fact that the ECG signal storage and transmission was excluded and thus a lower computational load to the processor was requested to the processor.

The obtained average values for the S/Nex percentage results in these cases are higher if compared with the correspondent running conditions with ECG signal storage and transmission active.

This difference is explainable in an increase of the computational resources disposable to execute the reading operations excluding the ECG signal storage and transmission and thus in a higher frequency of access to the RFCOMM serial buffer to get data frames.

If the reading operations occur more frequently a greater number of data package would be read.

Consequently if the elaboration chain from reading to storage has been testified to be reliable and the S/R has been found near to 100% , this means that the same packages are read the same are stored and so, if R increases then S increases and then S/Nex is higher.

In conclusion the results of the bench test lead to inference that even if the ShirtSIG System, and in particular the firmware installed on the DTS- the ShirtSIGCoder- is able to storage and transmit the data frames since they are read over the Bluetooth stream without data loss or corruption; the concomitant presence of the HMVSM installed compromises the reliability and the real-time features of the system.

On the basis of the analysis of the S/Nex values among the different running conditions tested, it can be inferred that the use of the ShirtSIG System together with HMVMS on the same Fox Board platform in the DTS is not reliable and do not guarantees a real time transmission of the signals from the shirt.

It can be hypothesized that the computational load of the concomitant execution of the both system's software is too high to be performed by ETRAX 100LX processor, installed on FOX Board.

Such conclusions can bring to consider the global project not consistent in its main idea but the results of the reliability test on long time and the pathological events recognition test can change the point of view of the problem.

By the results obtained from the reliability test on long time the ShirSIG system can be considered reliable on working for long time acquisitions, and thus for night time acquisitions: on 3 of 4 night on which it was tested to acquire for all night hours, the system worked properly sending and saving incoming data. No crashes neither problems have been reported.

The pathological events recognition test indeed -that has been conducted to analyse the ability of the system to show some pathological events typical of sleep disordered breathing and to provide significant additional information to the clinician for the remote titration-had shown how the use of the ShirtSIG System together with a software which acquires signals regarding the air flow dynamics from a mechanical ventilator allows a potential and useful improvement to the telemonitoring features, increasing the capability of the system to permit the clinician to remote titrate the ventilator following the patterns

and the abnormalities of the patient's breath in a more timely and personalized way.

During the test a simulation protocol studied to reproduce the most common breathing events related to chronic respiratory diseases during night time was performed by a healthy subject who wore the Chronious shirt and sustained a CPAP ventilation of 4 cmH2O through a nasal mask, generated by a PHILIPS Respironics BIPAP® SYNCHRONY® home mechanical ventilator.

The signal from the shirt was acquired by the ShirtSIG System and the signals from the ventilator were acquired by commercial software installed on an external laptop: the ventilator was connected to the laptop through an USB serial adapter to the laptop.

Considering the results of the bench test, the HMVMS was avoided to be installed on the DTS during this test to release computational load and to permit the ShirtSIGCoder to run in the best conditions.

The commercial software acquired the same signals acquired by the HMVMS software that are for the remote titration: they are air flow, pressure, volume and leaks from the nasal mask.

The protocol consisted in 3 acquisitions of 10 minutes each, structured as a set of periods of normal breathing followed by the occurrence of a simulated respiratory abnormality.

In the first acquisition the clinical conditions of the affection by obstructive sleep apnoeas syndrome have been simulated. The second acquisition simulates the central sleep apnoeas and finally the third provides chest-wall-abdomen asynchronies simulation, contracting the abdominal muscles and the diaphragm during inspiration.

The simulation test performed has shown how in particular the RIP signals – thorax and abdomen displacements and tidal volume – bring additional information on the movements of the chest-wall and the abdomen during breath.

This information has been found to permit a better discrimination of the different breathing disorder came out from the monitoring of the only air flow dynamics signals.

For example the presence of breathing movements of its absence during an apnoeic episode (flow and pressure decreased to zero) detectable from the RIP, resulted a distinctive feature between the obstructive and the central apnoeas simulated events.

With the acquisition of the RIP signals also the simulated chest-wall asynchronies has been immediately identified by the characteristic counter phase pattern between the thorax and abdomen displacements signals.

Moreover, the variations of the HR, ECG and SpO2 signals typical of each disorder brought efforts to the possibility to discriminate different breathing abnormalities.

In conclusion the main idea underlying the implementation of the global telemedicine system unifying the ShirtSIG System and the HMSVM can be considered consistent in the concept because additional information are practically brought or the remote titration by the signal of the shirt.

The main problem resides in the lack of computational load and thus in the hardware disposable to implement the idea.

The analysis on this problem can bring to review the project of the global telemedicine system which unify the ShirtSIG and HMVMS systems, opening the way to possible improvements of the original concept idea that regards the hardware and the software specifications.

Future improvements and developments are discussed in the following paragraph.

5.2 Future Developments

The main problem figured out from the test results is the lack of computational load disposable on the FOX Board to allow the execution of the software of both ShirtSIG System and HMVMS.

This matter limits the applications of the system in its clinical and practical use, at the actual state of development.

This problem can be solved implementing a more efficient firmware for ShirtSIGCode but also changing the hardware resources employed.

The Etrax LX100 processor on FOX Board LX 832 has been demonstrated to not be powerful enough to sustain the concomitant execution of the both system, but the realization of the global telemonitoring system by the unification of the ShirtSIG System and the HMVMS can be realized replacing the Fox Board LX 832 on the DTS with an embedded platform which guarantees a faster processor and in general more powerful computational resources.

Several embedded platforms that provide the same functionalities and services of the FOX Board but that support more powerful processors and memory resources are nowadays commercially available.

One of these devices is for example the FOX Board G20 produced by Acme Systems srl ® that is a Single Board Computer designed for embedded Linux; build around an Atmel ARM9 @ 400 MHz microprocessor.

This embedded platform is the upgraded version of the Fox Board LX 832 and its use can be a proposal improvement which allows to do not substantially modify the global structure of the ShirtSIG System.

The use of a more powerful platform for the DTS and thus a consequential more reliable implementation of the ShirtSIG System open the way to a better characterization of the system on working and clinical conditions.

The installation of a reliable station at patient home would permit further studies on the clinical effectiveness and utility of the system on real patients.

The tests conducted in this work has been limited in fact to only an healthy subject and no pathological subjects has been analyzed with the ShirtSIG System.

To better understand the effectiveness and the utility of the system, pilot studies on pathological subject should be performed.

Another possible improvement that can be implemented at the actual state of art regards the possibility to constitute an historical database of the recorded signals on the DTS.

The structure of the ShirtSIG System permits in the fact to decentralize the data storage of signal acquisition, from a huge database installed on specialist station to an SD memory a t patient's home.

The data storage process implemented for the ShirtSIG System could be reorganized in order to allow the remote consultation of historical tracks.

A remote database on the DTS memory could be realized and associated to a Web application that, once connected to the DTS, permits to select and visualize the tracks related to the historical acquisitions.

The potentiality of the ShirtSIG System as a telemonitoring system for the chronic respiratory diseases home care have not been fully explored in this thesis, but the original idea could be better developed on the basis of the results obtained in this work.

A telemedicine approach to the treatment of the respiratory diseases will acquire in the future an increasing importance, because it can respond in a cost-saving and personalized way to the increasing demand of respiratory health care.

Appendix A – Source Codes

hcid.conf

```
HCI daemon configuration file.
#
# $Id: hcid.conf,v 1.6 2004/10/26 02:31:22 holtmann Exp $
#

# HCId options
options {
      # Automatically initialize new devices
      autoinit yes;

      # Security Manager mode
      #   none - Security manager disabled
      #   auto - Use local PIN for incoming connections
      #   user - Always ask user for a PIN
      #
      security auto;

      # Pairing mode
      #   none  - Pairing disabled
      #   multi - Allow pairing with already paired devices
      #   once  - Pair once and deny successive attempts
      pairing multi;

      # PIN helper
      pin_helper /etc/bluetooth/mnt/flash/etc/bluetooth/pin;

      # D-Bus PIN helper
      #dbus_pin_helper;
}

# Default settings for HCI devices
device {
      # Local device name
      #   %d - device id
      #   %h - host name
      name "BlueZ (%d)";

      # Local device class
      class 0x3e0100;

      # Default packet type
      #pkt_type DH1,DM1,HV1;

      # Inquiry and Page scan
      iscan enable; pscan enable;
```

```
        # Default link mode
        #   none   - no specific policy
        #   accept - always accept incoming connections
        #   master - become master on incoming connections,
        #            deny role switch on outgoing connections
        #
        #lm accept,master;
        #
        lm accept;

        # Default link policy
        #   none    - no specific policy
        #   rswitch - allow role switch
        #   hold    - allow hold mode
        #   sniff   - allow sniff mode
        #   park    - allow park mode
        #
        #lp hold,sniff;
        #
        lp rswitch,hold,sniff,park;

        # Authentication and Encryption
        #auth enable;
        #encrypt enable;
}
```

blueinit.sh

```
#!/bin/sh
cdBluez-start
mount /dev/mmc0 /mnt/0 -t vfat -o noatime
mkdir /mnt/0/shirtdata
hcid -f /etc/bluetooth/hcid.conf
/mnt/flash/depackage&
```

config file

```
NomePaz=Device3
CognomePaz=Lares
NUM_PORT_FOX_SERVER=5870
PORT_NUM=5870
SERVER_IP=192.168.1.17
DATAHANDLER=00:80:25:14:A1:97
FOX_GATEWAY=10.48.92.254
AMP=154
GPRS_IP=10.48.92.8######
campo=74##
connessione=1
soglia=100
respironics=1
watchpoints=0
vent_acq=0
```

```
pulsossimetro=0
cavo=1
baudrate_ventilator=57600
versione_main=fox25_05_12
FINE
```

ShirtSIGCoder

shirtsigcoder.c

```
#include "framefunc.h"
#include "seriale.h"
#include "gprskit.h"
#include "blueconns.h"
#include "addons.h"


#define BR_seriale B115200
#define DEVICE "/dev/rfcomm0"
#define NUMTRIES 2000

/*log vars*/
int ecg_frames=0;
int pulsi_frames=0;
int respiframes=0;
int temp_frames=0;
int hr_frames=0;
int ecg_bytes=0;
int pulsi_bytes=0;
int respibytes=0;
int temp_bytes=0;
int hr_bytes=0;

/*saw bytes*/
unsigned char ecg_saw=0;
unsigned char respi_saw=0;
unsigned char pulsi_saw=0;
unsigned char temp_saw=0;

/*GPRS setting variables*/
char *SERVER_IP;
int SERVER_PORT;
int PORT_NUM;

/* GPRS comunication variables*/
int send_ctrl=0;
int ServerSKT=-1;
int ClientSKT=-1;
struct sockaddr_in ServerADDR,ClientADDR;
socklen_t addrlen = sizeof(struct sockaddr_in);
int retFXS;
int server=0;
int num_portfox;


/*command line controls*/
```

```
int display=0;
int ecgon=1;

/*serial bluetooth conn & check variables*/
int fd;
unsigned char start[13] =
{0xA8,0x0D,0x00,0x0A,0x0C,0x14,0x09,0x0F,0x00,0x00,0x20,0x17,0x5F};
unsigned char stop[13] =
{0xA8,0x0D,0x00,0x0A,0x0C,0x14,0x09,0x0F,0x00,0x00,0x21,0x18,0x60};
struct termios oldtio, newtio;
int bttries=0;
int timeout=500;
int read_length=60;
struct pollfd btds;
char *DATAHANDLER;

/*time and date variables*/
time_t rawtime;
struct tm * timeinfo;
char data[16];
char *dirdat;
char bindir[60];


/*files*/
FILE *file;

/*Send and connection check function*/
int send_w_check(int *Clsk,unsigned char* package,int dim);
int bluet_check();

int main(int argc, char* argv[])
{
/*Serial comunication variables*/
int i,ciclo,randint;
int ret=-1;

/*bytes and buffer_length*/
size_t byteletti;
int frame_length;
int buffer_length=200;
int residual_length=0;

/*buffers*/
unsigned char buffer_read[9000];
unsigned char proc_buffer[20000];
unsigned char buffer_bytestuffing[50];
unsigned char residual_buffer[10000];

if(GetStr(FILECONF,&SERVER_IP,"SERVER_IP")<0)
  {
    syslog(LOG_INFO,"Error in getting IP from file\n");
    exit(1);
  }

SERVER_PORT=5874;
PORT_NUM=5874;
if(GetStr(FILECONF,&DATAHANDLER,"DATAHANDLER")<0)
  {
```

```
    syslog(LOG_INFO,"Error in getting bt address from file\n");
    exit(1);
  }


/*initial control of bluetooth connection*/


syslog(LOG_INFO,"Waiting Datahandler connection....\n");
while(ret!=0)
 {
  bluet_check();
  ret=InitAcquisizione(&fd,&oldtio,&newtio,BR_seriale,DEVICE);
 }

syslog(LOG_INFO,"Initializing directories....\n");
/*dat storage directory initialization*/
time ( &rawtime );
timeinfo = localtime ( &rawtime );
srand(time(NULL));
randint=rand()%100;
sprintf (bindir,"%s%02d%02d%04d%02d%02d%02d%02d/",MAIN_DIR,timeinfo-
>tm_mday,timeinfo->tm_mon+1,1900+timeinfo->tm_year,timeinfo-
>tm_hour,timeinfo->tm_min,timeinfo->tm_sec,randint);
printf("Maindir:%s\n",bindir);
if(mkdir(bindir,0777)!=0)
{
  syslog(LOG_INFO,"Error in storage directory!\n");
  exit(1);
}

/*Serial Communication Initialization*/
if (ret==0)
      {
          write(fd,start,sizeof(unsigned char)*13);
        while(1)
         {
          ciclo++;
          if((server<=0))
            server=OpenServerSKT(&ServerSKT,&ServerADDR,SERVER_PORT);
            if(bluet_check())
            {
            ioctl(fd,FIONREAD,&read_length);
            if(read_length>0&&errno>=0&&read_length!=(-1))
            {
            byteletti=read(fd,&buffer_read[0],sizeof(unsigned
char)*read_length);
            buffer_length=byteletti+residual_length; //calcolo la nuova
lunghezza del buffer;
            memcpy(&proc_buffer[0],&residual_buffer[0],sizeof(unsigned
char)*residual_length);

memcpy(&proc_buffer[residual_length],buffer_read,sizeof(unsigned
char)*byteletti);
            residual_length=0;
            for(i=0;i<buffer_length;i++) //scanning data readed
             {
               if(proc_buffer[i]==0xA8)//start byte control
                 {
```

```
bytestuffing_remove(&proc_buffer[i],buffer_bytestuffing,45);
                  frame_length=get_length(buffer_bytestuffing,0); //read
length byte
                  if(frame_length>0) //check if length is greater that 0
                   {

      if(checksumtest(buffer_bytestuffing,frame_length))//checksumtest
                   {
                     /*Write data on file*/
                     if(ecgon==1)
                        {

      if(buffer_bytestuffing[11]==0x02||buffer_bytestuffing[11]==0x03||bu
ffer_bytestuffing[11]==0x05||buffer_bytestuffing[11]==0x00)
                           writeonfile(buffer_bytestuffing,frame_length);
                        }
                      else
                        {

      if(buffer_bytestuffing[11]==0x02||buffer_bytestuffing[11]==0x03||bu
ffer_bytestuffing[11]==0x05)
                           writeonfile(buffer_bytestuffing,frame_length);
                        }
                     /*Sending data on socket*/
                     if(server==1)
                       {
                          if (ClientSKT>0)
                             {

if(decodeGPRS(&buffer_bytestuffing[12],readtype(buffer_bytestuffing),deco
ded)>0)
                                    {

send_ctrl=send_w_check(&ClientSKT,decoded,15);
                                    }
                              }
                           else
                             {
                               ClientSKT=accept(ServerSKT,( struct
sockaddr *)&ClientADDR,&addrlen);
                                if (ClientSKT>0)
                                 {
                                  syslog(LOG_INFO,"Client Connected\n");

if(decodeGPRS(&buffer_bytestuffing[12],readtype(buffer_bytestuffing),deco
ded)>0)
                                    {

send_ctrl=send_w_check(&ClientSKT,decoded,15);
                                    };
                                 }
                              }
                        }
                     if((i+frame_length)<buffer_length)
                       i=i+frame_length-1;
                   }
                  else
                     {
```

```
                      if((buffer_length-i)<MIN_PACKAGE_LENGTH)
                      // if buffer end is smaller of minpackage length,
data will be copied in the residual buffer
                      {
                        residual_length=buffer_length-i;

memcpy(&residual_buffer[0],&proc_buffer[i],residual_length*sizeof(unsigne
d char));
                        /*jump residual length*/
                        if((i+residual_length)<buffer_length)
                        i=i+residual_length;
                      }
                      }
                    }
                  }
                }
              }
       if(logenable==1)
         writelog();
        }
        else
       {
        if(bttries>=NUMTRIES)
         goto abort;
        else
         sleep(1);
       }
      if(ciclo>20000)
       {
       time ( &rawtime );
       timeinfo = localtime ( &rawtime );
       syslog(LOG_INFO,"Timing:%02d%02d%04d-%02d:%02d:%02d,
Error:%d\n",timeinfo->tm_mday,timeinfo->tm_mon+1,1900+timeinfo-
>tm_year,timeinfo->tm_hour,timeinfo->tm_min,timeinfo->tm_sec,errno);
       ciclo=0;
       }
      }
abort:
      close(ClientSKT);
      close(ServerSKT);
      if(rawfile==1)
       fclose(file);
  }
}

int send_w_check(int *Clsk,unsigned char *package,int dim)
{
  int ctrl;
  ctrl=tcp_send(*Clsk,package,15);
  if(ctrl<0)
      {
        *Clsk= -1;
      }
  return ctrl;
}


int bluet_check()
{
```

```
 int initck;
 if(!isatty(fd)) //tests the presence of the device file pointed by fd
      {
        syslog(LOG_INFO,"DataHandler Disconnected,trying to connect\n");
        if(bttries<NUMTRIES)
          {
           close(fd);
           bind_bt(&fd,DATAHANDLER);

initck=InitAcquisizione(&fd,&oldtio,&newtio,BR_seriale,DEVICE);
           if(initck==0)
              {
                 syslog(LOG_INFO,"DataHandler Connected\n");
                 write(fd,start,sizeof(unsigned char)*13);
                 return 1;
            }
           else
              {

             syslog(LOG_INFO,"Error in trying to connect\n");
             bttries++;
             return -1;
              }
          }
        else
          {
           syslog(LOG_INFO,"Too many tries on DataHandler
reconnection,Operation Aborted\n");
           return -1;
          }
       }
 else
     {
       bttries=0;
       return 1;
     }
}
```

seriale.h

```
#include <sys/stat.h>
#include <fcntl.h>
#include <syslog.h>  // usata per scrivere i messaggi nei log messages

extern int display;


int InitSeriale(int *fd, struct termios *oldtio,struct termios
*newtio,tcflag_t baudrate, char *device);

int InitAcquisizione(int *fd,struct termios *oldtio, struct termios
*newtio,tcflag_t baudrate, char *device);
```

seriale.c

```
#include "seriale.h"
//*****************************************************************
************************************************
// INIT_SERIALE
// ritorna 0
// ritorna -1 se non è presente un dispositivo
//*****************************************************************
```

```
**************************************************
int InitSeriale(int *fd, struct termios *oldtio,struct termios
*newtio,tcflag_t baudrate, char *device)  //controllare tcflagt
{
            *fd = open(device, O_RDWR | O_NOCTTY | O_NONBLOCK );
            if (*fd < 0 )
            {
                  if (display==1)
                  {
                        printf("Device %s non presente su questo
sistema\n", device);
                  }
                  syslog(LOG_INFO,"Device %s non presente su questo
sistema\n", device);
                  return -1;
            }

            tcgetattr(*fd,oldtio);
            bzero(newtio, sizeof(*newtio));
            newtio->c_cflag = baudrate | CS8 | CLOCAL | CREAD;
            newtio->c_iflag = IGNPAR;
            newtio->c_oflag = 0;
            newtio->c_lflag = 0;
            newtio->c_cc[VTIME] = 0;
            newtio->c_cc[VMIN] = 1;
            tcflush(*fd, TCIFLUSH);
            tcsetattr(*fd,TCSANOW,newtio);
            return 0;
}


//**************************************************************************
*****************************
// INIT_ACQUISIZIONE
// ritorna -1 se si è verificato un errore di comunicazione con la
seriale
// ritorna 0 se è andato tutto bene
//**************************************************************************
*****************************
int InitAcquisizione(int *fd, struct termios *oldtio, struct termios
*newtio,tcflag_t baudrate, char *device)
{
            //int i;
            int y;
            //char buf[200];

            if(InitSeriale(fd,oldtio,newtio,baudrate,device)<0)
            {
                  if (display==1)
                  {
                        printf("ERRORE nella comunicazione seriale\n");
                  }
                  syslog(LOG_INFO,"ERRORE nella comunicazione
seriale\n");
                  return -1;
            }
```

```
            for(y=0;y<60000;y++);
            return 0;
}
```

framefunc.h

```
#include "conio.h"
#include <string.h>
#include <stdlib.h>
#include <errno.h>
#include <stdio.h>
#include <pthread.h>
#include <termios.h>
#include <unistd.h>
#include <syslog.h>
#include <sys/ioctl.h>
#include <time.h>

#define LENGTH_ECG 6
#define LENGTH_RespiSENS 18
#define LENGTH_PULSI 2
#define LENGTH_TEMP 6


#define DATIGREZZI "/mnt/0/datigrez.bin"
#define MAIN_DIR "/mnt/0/shirtdata/"

#define ECG_FILE "ECG.bin"
#define HR_FILE "HR.bin"
#define RespiSENS_FILE "RespiSENSE.bin"
#define PULSI_FILE "PULSI.bin"
#define TEMP_FILE "TEMP.bin"
#define MIN_PACKAGE_LENGTH 16
#define MAX_PACKAGE_LENGTH 33
#define ECG_TIMELINE "ecg_time.txt"
#define RESPI_TIMELINE "respi_time.txt"
#define PULSI_TIMELINE "pulsi_time.txt"
#define TEMP_TIMELINE "temp_time.txt"

/*command line variables*/
extern int display;
extern int logenable;
extern int ClientSKT;

/*package counter variables*/
/*bluetooth*/
extern int ecg_frames;
extern int pulsi_frames;
extern int respiframes;
extern int temp_frames;
extern int hr_frames;
extern int ecg_bytes;
extern int pulsi_bytes;
extern int respibytes;
extern int temp_bytes;
extern int hr_bytes;
```

```
/*decoded*/
extern int ecg_decoded;
extern int pulsi_decoded;
extern int respidecoded;
extern int temp_decoded;
extern int hr_decoded;

/*saw bytes*/
extern unsigned char ecg_saw;
extern unsigned char respi_saw;
extern unsigned char pulsi_saw;
extern unsigned char temp_saw;


/*time*/
extern char bindir[60];
/*extern char timedir[60];*/
extern int ecgon;



typedef struct timestamp
{
 unsigned year:16;
 unsigned month:8;
 unsigned day:8;
 unsigned hour:8;
 unsigned minutes:8;
 unsigned seconds:8;
 unsigned milli:8;
}t_timestamp;

int bytestuffing_remove(unsigned char *bufferin,unsigned char
*bufferout,int sizebuff_in);

int get_lenght(unsigned char *bufferin,int i);

unsigned char *copy_buffer(unsigned char *bufferin, unsigned char
*framebuffer,int pos_buffer,int pos_frame,int length);

int checksumtest(unsigned char *framebuffer, int length);

void timestamp_read(unsigned char *framebuffer,t_timestamp *timestamp);

unsigned char readtype(unsigned char *framebuffer);

int writeonfile(unsigned char *frame,int frame_length);

void update_log(int numbyte,unsigned char type);

unsigned char sawincr(unsigned char sawbyte);

void log_sendt(unsigned char type);

void log_decoded(unsigned char type);

int decodeGPRS(unsigned char *dataframe,unsigned char type,unsigned char*
retvalue);
```

framefunc.c

```
// Required header files
#include "framefunc.h"
//*****************************************************************
*************************************************
// BYTESTUFFING_REMOVE
// remove bytestuffing bytes
//*****************************************************************
*************************************************

int bytestuffing_remove(unsigned char *bufferin,unsigned char
*bufferout,int sizebuff_in)
{ int i,j;
  i=0;
  j=0;
  while(i<sizebuff_in)
       {
       if
((bufferin[i]==0xA9&&bufferin[i+1]==0x88)||(bufferin[i]==0xA9&&bufferin[i
+1]==0x89))
          {
            if (bufferin[i]==0xA9&&bufferin[i+1]==0x88)
             bufferout[j]=0xA8;
            if (bufferin[i]==0xA9&&bufferin[i+1]==0x89)
             bufferout[j]=0xA9;
              i++;
          }
       else
          {
           bufferout[j]=bufferin[i];
          }
       i++;
       j++;
       }
  return j;
}


//*****************************************************************
*************************************************
// GET_LENGTH
//received the input buffer and the posizion of the stream return the
length of the dataframe
//*****************************************************************
*************************************************

int get_length(unsigned char *bufferin,int pos)
{
int MSB,LSB,length;
LSB=bufferin[pos+1];
MSB=bufferin[pos+2];
MSB=MSB<<8;
length=MSB+LSB;
if(length>MAX_PACKAGE_LENGTH||length<MIN_PACKAGE_LENGTH) //controllo
sulla lunghezza del pacchetto
  return -1;
else
  return length;
```

```
}

//*************************************************************************
**************************************************
// COPY_FRAME_BUFFER
//copy a buffer to another
//*************************************************************************
**************************************************


unsigned char*copy_buffer(unsigned char *bufferin, unsigned char
*framebuffer,int pos_buffer,int pos_frame, int length)
{
int i;
int j=pos_buffer;
for (i=pos_frame;i<length;i++) //copio i contenuti
  {
    framebuffer[i]=bufferin[j];
    j++;
  }
return framebuffer;
}


//*************************************************************************
**************************************************
// CHECKSUMTEST
// Check Checksum bytes
//returns 1 if Ok
//ritorna 0 if failed
//*************************************************************************
**************************************************


int checksumtest(unsigned char *framebuffer, int length)
{
int i;
unsigned char t_CS1,t_CS2;
t_CS1=0;
t_CS2=0;
for (i=0;i<length-2;i++) //calcolo i valori di Checksum teorici
  {
    if(t_CS1>0xFF)
      {
      t_CS1=0;
      }
    if(t_CS2>0xFF)
      {
      t_CS2=0;
      }
    t_CS1=t_CS1+framebuffer[i];
    t_CS2=t_CS2+t_CS1;
  }
if((t_CS1==framebuffer[length-2])&&(t_CS2==framebuffer[length-1])) //
  return 1;
else
  return 0;
}
```

```
//*****************************************************************************
**************************************************
// READTYPE
// Read Dataframe type
//*****************************************************************************
**************************************************

unsigned char readtype(unsigned char *framebuffer)
{
return framebuffer[11];
}

//*****************************************************************************
**************************************************
// SAWINCR
// Increase saw counter
//*****************************************************************************
**************************************************

unsigned char sawincr(unsigned char sawbyte)
{
 if(sawbyte+1>255)
   sawbyte=0;
 else
   sawbyte++;
 return sawbyte;
}

//*****************************************************************************
**************************************************
// TIMESTAMP READ
// Reads dataframe timestamp
//*****************************************************************************
**************************************************

void timestamp_read(unsigned char *framebuffer,t_timestamp *timestamp)
{
 timestamp->year=(int)framebuffer[3]+2000;
 timestamp->month=(unsigned int)framebuffer[4];
 timestamp->day=(unsigned int)framebuffer[5];
 timestamp->hour=(unsigned int)framebuffer[6];
 timestamp->minutes=(unsigned int)framebuffer[7];
 timestamp->seconds=(unsigned int)framebuffer[8];
 timestamp->milli=(unsigned int)framebuffer[9];
}



//*****************************************************************************
******************************
// LOG_DECODED
//log file update
//
//*****************************************************************************
******************************
void log_decoded(unsigned char type)
{
 switch (type)
  {
```

```
      case 0x00://ECG
      {
       ecg_decoded++;
       break;
      }
      case 0x02://RespiSENS Data
      {
       respidecoded++;
       break;
      }
      case 0x03://Pulsi
      {
       pulsi_decoded++;
       break;
      }
      case 0x04://Audio
      {
       break;
      }
      case 0x05://Temperature&Humidity
      {
       temp_decoded++;
       break;
      }
      case 0x06://Report
      {
       break;
      }
      case 0x07://Activity Change Data
      {
       break;
      }
      case 0x10://Event Status
      {
       break;
      }
      case 0x11://Sensor Status
      {
       break;
      }
      default:
      {
       break;
      }
   }
}



//*************************************************************************
*****************************
// DECODEGPRS
// realize data frame compression
//
//*************************************************************************
*****************************

int decodeGPRS(unsigned char *dataframe,unsigned char type,unsigned char*
retvalue)
```

```
{
 int MSB,LSB,i;
 unsigned char *sawbyte;
 int exp_core_length;//lunghezza attesa del pacchetto
 switch (type)
  {
       case 0x00://ECG
      {
       if(ecgon==1)
       {
       retvalue[5]=0x03;
       sawbyte=&ecg_saw;
       exp_core_length=6;
       }
       else
         return -1;
       break;
      }
      case 0x01://ECG HR
      {
        return -1;
        break;
      }
      case 0x02://RespiSENSE Data
      {
       retvalue[5]=3;
       sawbyte=&respi_saw;
       exp_core_length=6;
       break;
      }
      case 0x03://Pulsi
      {
       retvalue[5]=2;
       sawbyte=&pulsi_saw;
       exp_core_length=2;
       break;
      }
      case 0x05://Temperature&Humidity
      {
       retvalue[5]=3;
       sawbyte=&temp_saw;
       exp_core_length=6;
       break;
      }
      default:
      {
       return -1;
       break;
      }
   }
   /*retvalue[0]=0xFF;
   retvalue[1]=0xFF;
   retvalue[2]=0xFF;
   retvalue[3]=0xFF;*/
   retvalue[4]=type;
   memcpy(&retvalue[6],&dataframe[0],exp_core_length*sizeof(unsigned
char));
   memcpy(&retvalue[13],sawbyte,sizeof(unsigned char));
```

```
   if(logenable==1)
    log_decoded(retvalue[4]);
   return 2;
}



//*********************************************************************
*****************************
// WRITEONFILE
// Write on the storage file the data frame
//
//*********************************************************************
*****************************

int writeonfile(unsigned char *frame,int frame_length)
{
 char nomefile[60];
 char timeline[60]="null.txt";
 FILE *recfile,*timefile;
 int i;
 //unsigned char data_core[50];
 t_timestamp time;
 unsigned char *sawbyte;
 int numbyte_write;
 int exp_core_length;//lunghezza attesa del pacchetto
 strcpy(nomefile,bindir);
 strcpy(timeline,bindir);
 switch (readtype(frame))
  {
      case 0x00://ECG
      {
       strcat(nomefile,ECG_FILE);
       strcat(timeline,ECG_TIMELINE);
         exp_core_length=6;
       ecg_frames++;
       ecg_saw=sawincr(ecg_saw);
       sawbyte=&ecg_saw;
       break;
      }
      case 0x01://ECG HR
      {
         return -1;
       break;
      }
      case 0x02://RespiSENS Data
      {
       strcat(nomefile,RespiSENS_FILE);
       strcat(timeline,RESPI_TIMELINE);
         exp_core_length=6;
       respiframes++;
       respi_saw=sawincr(respi_saw);
       sawbyte=&respi_saw;
       break;
      }
      case 0x03://Pulsi
      {
       strcat(nomefile,PULSI_FILE);
       strcat(timeline,PULSI_TIMELINE);
```

```
          exp_core_length=2;
        pulsi_frames++;
        pulsi_saw=sawincr(pulsi_saw);
        sawbyte=&pulsi_saw;
        break;
       }
       case 0x05://Temperature&Humidity
       {
        strcat(nomefile,TEMP_FILE);
        strcat(timeline,TEMP_TIMELINE);
        exp_core_length=6;
        temp_frames++;
        temp_saw=sawincr(temp_saw);
        sawbyte=&temp_saw;
        break;
       }
       default:
       {
        return -1;
        break;
       }

   }
   //scrittura su file
  // memcpy(&data_core[0],&frame[12],exp_core_length*sizeof(unsigned
char));
   //printf("Sawbyte:%d\n",*sawbyte);
   timestamp_read(frame,&time);
   if(frame_length<exp_core_length)
      {
        printf("\nErrore pacchetto troppo corto");
        return -1;
      }
   else
     {
        recfile=fopen(nomefile,"ab");
        numbyte_write=fwrite(&frame[12],sizeof(unsigned
char),exp_core_length,recfile);
       fwrite(sawbyte,sizeof(unsigned char),1,recfile);
       if(logenable==1)
        update_log(numbyte_write,readtype(frame));
        timefile=fopen(timeline,"a");
       fprintf(timefile,"%d-%d-%d,
%d:%d:%d.%d\n",time.year,time.month,time.day,time.hour,time.minutes,time.
seconds,time.milli);
       fclose(timefile);
       fclose(recfile);
       return exp_core_length;

       }
}

//*************************************************************************
*****************************
// UPDATE_LOG
// updates log counters
//
//*************************************************************************
*****************************
```

```
void update_log(int numbyte,unsigned char type)
{
 switch (type)
  {
      case 0x00://ECG
      {
       ecg_bytes=ecg_bytes+numbyte;
       break;
      }
      case 0x01://ECG HR
      {
       hr_bytes=hr_bytes+numbyte;
       break;
      }
      case 0x02://RespiSENS Data
      {
       respibytes=respibytes+numbyte;
       break;
      }
      case 0x03://Pulsi
      {
       pulsi_bytes=pulsi_bytes+numbyte;
       break;
      }
      case 0x04://Audio
      {
       break;
      }
      case 0x05://Temperature&Humidity
      {
       temp_bytes=temp_bytes+numbyte;
       break;
      }
      case 0x06://Report
      {
       break;
      }
      case 0x07://Activity Change Data
      {
       break;
      }
      case 0x10://Event Status
      {
       break;
      }
      case 0x11://Sensor Status
      {
       break;
      }
      default:
      {
       break;
      }
   }

}
```

```
//*********************************************************************
*****************************
// WRITE LOG
// updates log file
//
//*********************************************************************
*****************************

void writelog()
{
 FILE *logfile;
 logfile=fopen("/mnt/flash/log.txt","w+");
 fprintf(logfile,"Frames:\nECG frames:%d\nResp frames:%d\nPulsi
frames:%d\nTemp&Humidity
frames:%d\n",ecg_frames,respiframes,pulsi_frames,temp_frames);
 fprintf(logfile,"Total Bytes:\nECG bytes:%d\nResp bytes:%d\nPulsi
bytes:%d\nTemp&Humidity
bytes:%d\n",ecg_bytes,respibytes,pulsi_bytes,temp_bytes);
 fprintf(logfile,"Decoded:\nECG sendt:%d\nResp sendt:%d\nPulsi
sendt:%d\nTemp&Humidity
sendt:%d\n",ecg_decoded,respidecoded,pulsi_decoded,temp_decoded);
fclose(logfile);
}
```

gprskit.h

```
#include <sys/types.h>
#include <sys/socket.h>
#include <sys/poll.h>
#include <fcntl.h>
#include <errno.h>
#include <syslog.h>
#include <netinet/in.h>
#include <arpa/inet.h>
#include <asm/etraxgpio.h>


extern char *SERVER_IP;
extern int display;

int tcp_send(int sktclnt,unsigned char *dato,int num_can);

int OpenServerSKT(int*Server_SKT,struct sockaddr_in *Server_ADDR,int
NUM_PORT_SERVER);
```

gprskit.c

```
#include "gprskit.h"

//*********************************************************************
***********************************
// TCP_send
// transmitt data on tcp socket
//*********************************************************************
***********************************
int tcp_send(int sktclnt,unsigned char *dato,int num_can)
{
```

```
    int ret=0;
    int pkgctrl=0;
    unsigned int canale, i;
    struct pollfd ufds;
    ufds.fd=sktclnt;
    ufds.events=POLLOUT | POLLERR;  //controllo se posso spedire
    ret=poll(&ufds, 1, 1);
    if(!(ufds.revents & POLLOUT)) //significa !=1, se questa parentesi è
uguale a 1 vuol dire che si può scrivere sul dispositivo relativo.
      {
         syslog(LOG_INFO,"Send error, client disconnected\n");
       return -1;
      }
     for(i=0;i<num_can;i++)
      {
        ret=poll(&ufds, 1, 1);
        if(!(ufds.revents & POLLOUT)) //significa !=1, se questa
parentesi è uguale a 1 vuol dire che si può scrivere sul dispositivo
relativo.
        {
            syslog(LOG_INFO,"Send error,package lost\n");
            shutdown(sktclnt,2);
            return -1;
        }
        else
        {
          canale=*(dato+i);
          ret=send(sktclnt,&canale,(int)sizeof(unsigned char),0);
          if(ret==-1)
          {
              syslog(LOG_INFO,"Send error,package lost\n");
              return -1;
          }
        }
       }
    return 0;

}

//*************************************************************************
*************************************************************************
****************************************
// OpenServerSKT
// starts the server and creates the socket
// returns -2 e -1 in case of error
//*************************************************************************
*************************************************************************
****************************************

int OpenServerSKT(int *Server_SKT,struct sockaddr_in *Server_ADDR,int
NUM_PORT_SERVER)
{
     if (display==1)
        printf("Server Starting on Fox\n");
     syslog(LOG_INFO,"Server Starting on Fox\n");
     *Server_SKT = socket(AF_INET, SOCK_STREAM, 0); //apertura socket
     if ((*Server_SKT = socket(AF_INET, SOCK_STREAM, 0))< 0)
        {
        if(display==1)
```

```
          error("ERROR opening socket:%d",errno);
        syslog(LOG_INFO,"ERROR opening socket:%d",errno);
          return -1;
        }
     else
       {
      fcntl(*Server_SKT,F_SETFL,O_NONBLOCK);
      Server_ADDR->sin_family = AF_INET;
      Server_ADDR->sin_port = htons(NUM_PORT_SERVER);
      Server_ADDR->sin_addr.s_addr=inet_addr(SERVER_IP);
      if (bind(*Server_SKT,(struct sockaddr
*)Server_ADDR,sizeof(*Server_ADDR)) < 0)  //binding del socket
          {
            if(display==1)
            error("ERROR on binding Server:%d\n",errno);
            syslog(LOG_INFO,"ERROR on binding Server:%d\n",errno);
            return -2;
           }
      else
           {
          listen(*Server_SKT,3); //socket in ascolto
          if(display==1)
            printf("Server Opened on %d address
%s\n",NUM_PORT_SERVER,SERVER_IP);
          syslog(LOG_INFO,"Server Opened on %d address
%s\n",NUM_PORT_SERVER,SERVER_IP);
         }
        }
     return 1;
}
```

blueconns.h

```
#include <sys/socket.h>
#include <sys/wait.h>
#include <errno.h>
#include <stdio.h>
#include <sys/ioctl.h>
#include "bluetooth.h"
#include "hci.h"
#include "hci_lib.h"
#include "rfcomm.h"

extern int fd;
extern int display;

static int create_dev(int ctl,int dev,uint32_t flags,bdaddr_t
*bdaddr,char *s);

static int __other_bdaddr(int s, int dev_id, long arg);
int hci_for_each_dev(int flag, int (*func)(int s, int dev_id, long arg),
long arg);
int hci_open_dev(int dev_id);
int hci_get_route(bdaddr_t *bdaddr);

int bind_bt(int *st,char *strba);
int bluezconn_client(int *sock,int channel);
int bluezconn_serv(int *sck,int ch);
```

blueconns.c

```
#include "blueconns.h"

/* HCI functions that do not require open device */
static int __other_bdaddr(int s, int dev_id, long arg)
{
      struct hci_dev_info di = {dev_id: dev_id};
      if (ioctl(s, HCIGETDEVINFO, (void *) &di))
            return 0;
      return bacmp((bdaddr_t *) arg, &di.bdaddr);
}


int hci_for_each_dev(int flag, int (*func)(int s, int dev_id, long arg),
long arg)
{
      struct hci_dev_list_req *dl;
      struct hci_dev_req *dr;
      int dev_id = -1;
      int s, i;

      s = socket(AF_BLUETOOTH, SOCK_RAW, BTPROTO_HCI);
      if (s < 0)
            return -1;

      dl = malloc(HCI_MAX_DEV * sizeof(*dr) + sizeof(*dl));
      if (!dl) {
            close(s);
            return -1;
      }

      dl->dev_num = HCI_MAX_DEV;
      dr = dl->dev_req;

      if (ioctl(s, HCIGETDEVLIST, (void *)dl))
            goto done;

      for (i=0; i < dl->dev_num; i++, dr++) {
            if (hci_test_bit(flag, &dr->dev_opt))
                  if (!func || func(s, dr->dev_id, arg)) {
                        dev_id = dr->dev_id;
                        break;
                  }
      }

done:
      close(s);
      free(dl);
      return dev_id;
}

int hci_get_route(bdaddr_t *bdaddr)
{
      if (bdaddr)
            return hci_for_each_dev(HCI_UP, __other_bdaddr, (long)
bdaddr);
      else
```

```
            return hci_for_each_dev(HCI_UP, NULL, 0);
}


/* Open HCI device.
 * Returns device descriptor (dd). */
int hci_open_dev(int dev_id)
{
      struct sockaddr_hci a;
      int dd, err;

      /* Create HCI socket */
      dd = socket(AF_BLUETOOTH, SOCK_RAW, BTPROTO_HCI);
      if (dd < 0)
            return dd;

      /* Bind socket to the HCI device */
      a.hci_family = AF_BLUETOOTH;
      a.hci_dev = dev_id;
      if (bind(dd, (struct sockaddr *) &a, sizeof(a)) < 0)
            goto failed;

      return dd;

failed:
      err = errno;
      close(dd);
      errno = err;
      return -1;
}



static int create_dev(int ctl,int dev,uint32_t
flags,bdaddr_t*bdaddr,char*strba)
{
  struct rfcomm_dev_req req;
  int err;
  memset(&req,0,sizeof(req));
  req.dev_id = dev;
  req.flags = flags;
  bacpy(&req.src,bdaddr);
  str2ba(strba,&req.dst);
  req.channel=1;
  ioctl(ctl,RFCOMMRELEASEDEV,&req);
  err = ioctl(ctl,RFCOMMCREATEDEV,&req);
  if (err == EOPNOTSUPP)
    {
      if(display==1)
      printf("RFCOMM TTY support not available\n");
      return err;
    }
  else if (err < 0)
    {
      if(display==1)
      perror("Can't create device");
      return err;
    }
  else
```

```
    return 0;
}


int bind_bt(int *st,char *strba)
{
  close(*st);
  bdaddr_t bdaddr;
  int i, opt, dev_id, show_all = 0, err,devsk;
  FILE *devfile;
  bacpy(&bdaddr, BDADDR_ANY);
  *st = socket(AF_BLUETOOTH, SOCK_RAW, BTPROTO_RFCOMM);
  if (*st < 0)
    {
      if (display==1)
      perror("Can't open RFCOMM control socket");
      exit(1);
    }
  dev_id = atoi ("/dev/rfcomm0");
  /*create Device*/
  err = create_dev(*st, dev_id, 0, &bdaddr, strba);
  return err;
}


int bluezconn_client(int *sock,int channel)
 {

    struct sockaddr_rc addr = { 0 };
    int s, status;
    char dest[18] = "00:80:25:14:A0:89";
    // allocate a socket
    *sock = socket(AF_BLUETOOTH, SOCK_STREAM, BTPROTO_RFCOMM);
    printf("Socket:%d\n",*sock);
    // set the connection parameters (who to connect to)
    addr.rc_family = AF_BLUETOOTH;
    addr.rc_channel = (uint8_t)channel;
    str2ba(dest,&addr.rc_bdaddr);
    printf("Connection to:%s\n",dest);
    status = connect(*sock,(struct sockaddr *)&addr,sizeof(addr));
    printf("Errno:%d",errno);
    // send a message
    if( status == 0 )
      {
      return 0;
      }
    if( status < 0 )
      {
      printf("Not Connected!");
      close(s);
      return -1;
      }
}


int bluezconn_serv(int *sck,int ch)
 {
    struct sockaddr_rc loc_addr = { 0 }, rem_addr = { 0 };
    char dest[18] = "00:80:25:14:A0:89";
```

```
    int s;
    socklen_t opt = sizeof(rem_addr);

    // allocate socket
    s = socket(AF_BLUETOOTH, SOCK_STREAM, BTPROTO_RFCOMM);

    // bind socket to port 1 of the first available
    // local bluetooth adapter
    loc_addr.rc_family = AF_BLUETOOTH;
    loc_addr.rc_bdaddr = *BDADDR_ANY;
    loc_addr.rc_channel = (uint8_t) ch;
    bind(s, (struct sockaddr *)&loc_addr, sizeof(loc_addr));
    // put socket into listening mode
    listen(s, 1);

    // accept one connection
    *sck = accept(s, (struct sockaddr *)&rem_addr, &opt);

    ba2str( &rem_addr.rc_bdaddr, dest );
    printf("accepted connection from %s\n", dest);
    memset(dest, 0, sizeof(dest));
 }
```

addons.h

```
#include <stdio.h>
#include <time.h>
#include <string.h>
#include <stdlib.h>
#include <syslog.h>  // usata per scrivere i messaggi nei log messages


extern int display;

#define FILECONF "/mnt/flash/config"

int GetStrF(char **parametro,char *NomePar, FILE*pFile);

int GetStr(char*nomefile, char **parametro,char *NomePar);

int EseguiComando(char *comando);
```

addons.c

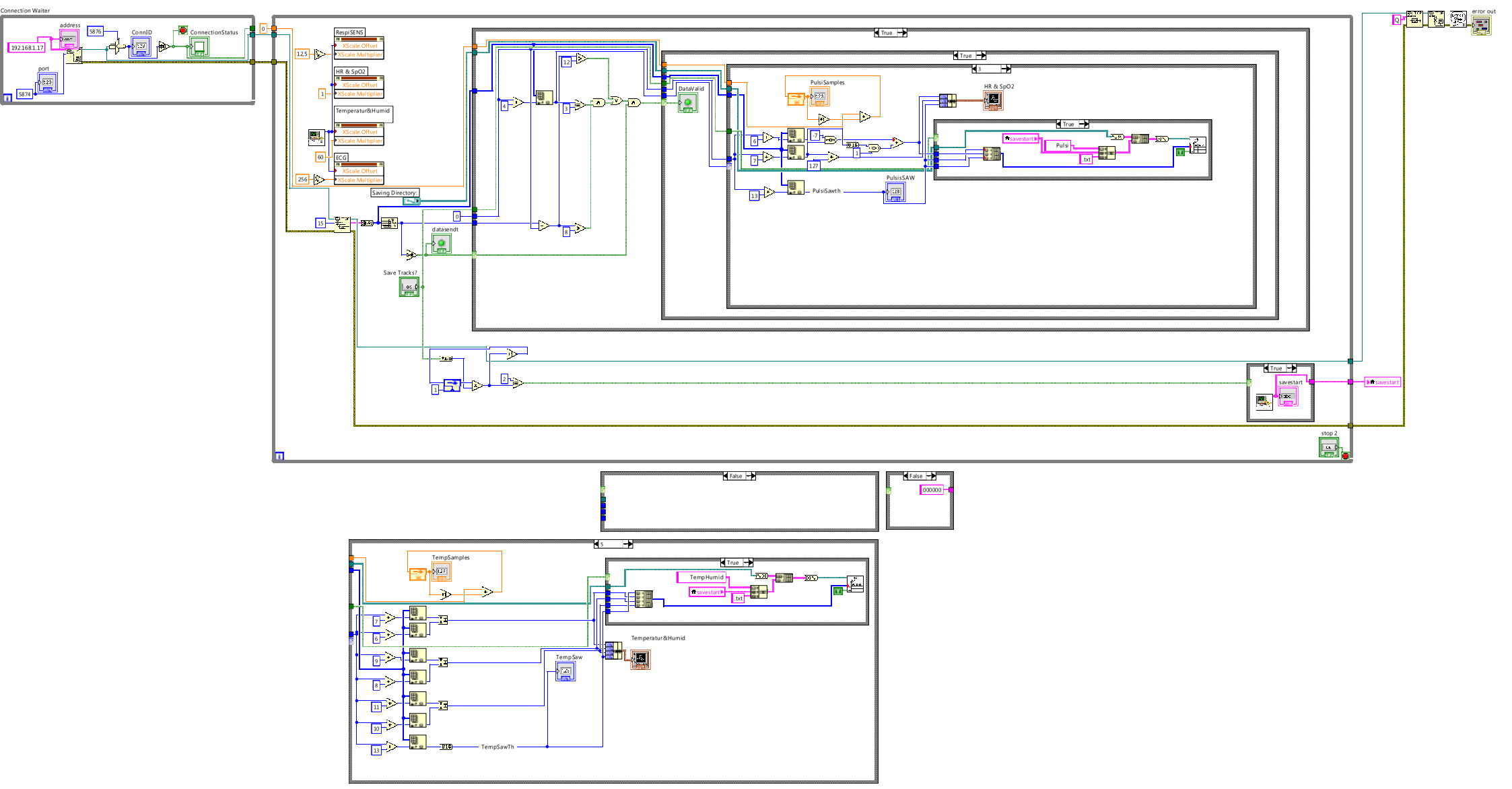
```
#include "addons.h"
//*****************************************************************
**********************************************************
// GET_STR_F
//*****************************************************************
**********************************************************
int GetStrF(char **parametro,char *NomePar, FILE*pFile)
{
            char s[60];
            char s2[60];
            while (feof(pFile)==0)
            {
                  fscanf(pFile, "%s", s );
                  char *p2=strchr(s, '='); //estraggo ciò che sta a sx
dell'=
```

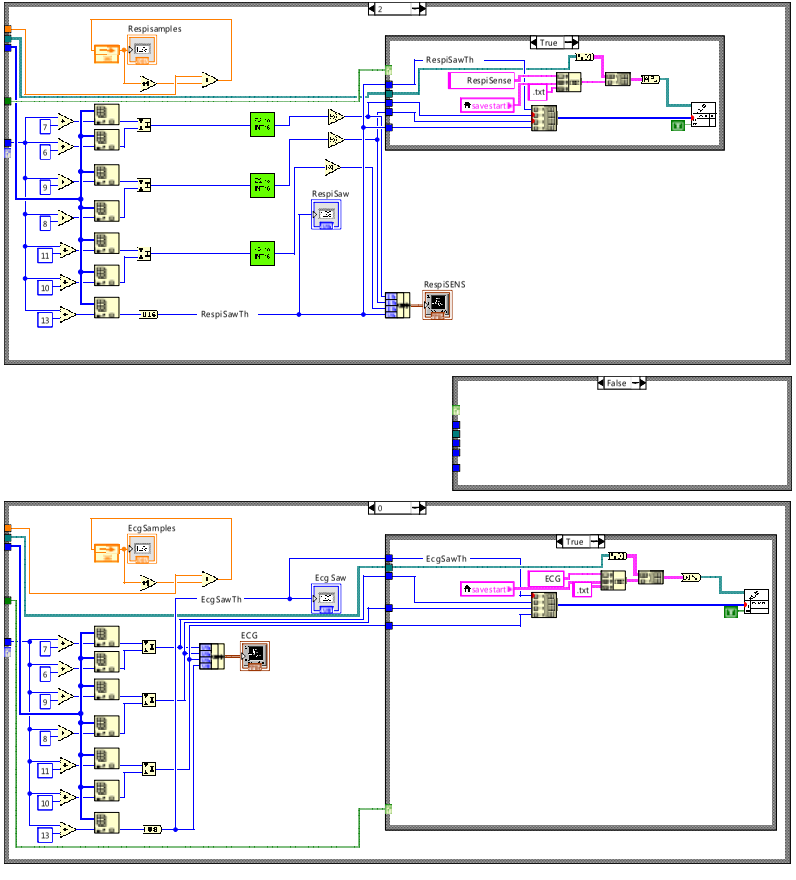
```
                  strncpy(s2,s,((unsigned int) p2) -((unsigned int) s));
                  if (  strncmp(s2,NomePar,((unsigned int) p2) -
((unsigned int) s))==0 &&(((unsigned int) p2) -((unsigned int)
s)==strlen(NomePar)))
                  {
                        //se ho trovato il parametro giusto leggo quello
che si trova a destra dell'=
                              (*parametro)=(char* ) malloc(60);
                  strcpy((*parametro),(char*) (((unsigned int) p2)+1));
                  strcpy((*parametro),(char*) (((unsigned int) p2)+1));
                        return 0;
                  }
            }

            return -2;
}


//*********************************************************************
*************************************************
// GET_STR
//*********************************************************************
*************************************************
int GetStr(char*nomefile, char **parametro,char *NomePar)
{
            FILE*pFile;
            pFile=fopen (nomefile, "rt");
            if(pFile==NULL)
      {
            if (display==1)
                  {
                        printf("Errore di apertura del file %s\n",
nomefile);
                  }
            return -1;
      }

            int r=GetStrF(parametro,NomePar,pFile);
            fclose(pFile);
            return r;
}
//*********************************************************************
*************************************************
// ESEGUI COMANDO
//*********************************************************************
*************************************************

int EseguiComando(char *comando)
{
      int pid;
      pid=fork();
      if (pid==0)
      {
            //syslog(LOG_INFO,"Eseguo il comando %s.",comando);
            system(comando);
            exit(EXIT_SUCCESS);
      }
      return 0;
}
```

Appendix B

ShirtSIGViewer.vi

Block Diagram


Connection Waiter
address
192.168.1.17
5876
ConnID
ConnectionStatus
port
5874
RespiSENS
XScale.Offset
XScale.Multiplier
HR & SpO2
Temperatur&Humid
ECG
Saving Directory
datasendt
Save Tracks?
DataValid
PulsiSamples
HR & SpO2
PulsisSAW
PulsiSawth
savestart
Pulsi
.txt
stop 2
error out
TempSamples
TempHumid
Temperatur&Humid
TempSaw
TempSawTh
False
000000


Respisamples
2
True
RespiSawTh
RespiSense
savestart
txt
RespiSaw
RespiSENS
RespiSawTh
False
0
EcgSamples
True
EcgSawTh
Ecg Saw
EcgSawTh
ECG
savestart
ECG
txt

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