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Abstract. Cardiovascular diseases remain the leading cause of morbidity, mortality, early disability and growing health costs worldwide. The difficulty for monitoring the evolution of cardiovascular related diseases can be, partially, attributed to the lack of appropriate indicators for arterial injury and cardiac disfunction during routine clinical practice. Non-invasive sensors, such as Photoplethysmography (PPG) devices, can be used for the measurement of several hemodynamic related parameters, albeit, most of current sensors require a skilled operator to interpret that sensory data. This paper presents a novel, method for an open architecture system where the simultaneous utilization of different types of devices is possible, PPG, Electrocardiogram (ECG) or other. Working, communicating and synchronizing through a wireless network, those can be placed on specific points of the patient's body and will allow to get better information of the cardiovascular marker of interest: hemodynamic or other, reducing the workload for the operator. The proposed open architecture is a simple cost-effective solution that can potentially achieve a widespread use in daily clinical practice.practice.

Keywords: Wireless Sensors Networks (WSN), Synchronization Protocols, Photoplethysmography (PPG), Health Diagnosis, Cardiovascular Markers.

1 Introduction

Cardiovascular diseases (CVDs), remain the leading cause of morbidity, mortality, early disability and growing health costs worldwide. In response to this crisis the world health organization (WHO) proposed a global plan for prevention and control of Noncommunicable Diseases (NCDs) 2013-2020 [1]. Where, one of the key points states that, as a part of a global risk mitigation program for CVDs, prevention should come from a total cardiovascular risk assessment approach; this being achieved during routine clinical practice. The difficulty for monitoring the evolution of cardiovascular related diseases during the routine clinical practice can be, to some extent, attributed to the lack of appropriate indicators for arterial injury and cardiac disfunction that can be readily, reliably and cheaply used. Non-invasive sensors, such as doppler ultrasound, magnetic resonance imaging (MRI), photoplethysmography (PPG) and cuff oscillometer devices, can be used for the detection and measurement of several hemodynamics and vascular stiffness related parameters, such as pulse wave velocity (PWV). The pulse wave velocity parameter can be calculated with a good degree of precision using the referred methods, albeit not all use the same working principles; ultrasound and magnetic resonance imaging use the pressure-and-volume and the pressure-and-diameter principle [2]. PPG and cuffs are typically used in pairs to simultaneously measure the travel time of the observed blood pressure wave in different body locations, thus deriving the value of the PWV velocity [3]. Figure 1 shows the points on the human body that are usually selected for those measurements.

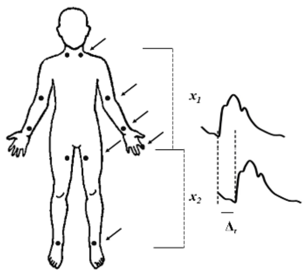

Fig. 1. Typical points of interest that can be used for PWV evaluation (left), and signal pulse wave difference at two monitoring locations (right). (Source: author, adapted from CCBY 3.0).

Equation (1) describes the general principle for the calculation of the PWV measuring the difference of blood pulse wave travel time between two points, for PPG and cuff type devices, [2].

$$PWV = \frac{\Delta x}{\Delta t} \quad (1)$$

The complexity and costs of using anyone of these methods can vary significantly by type; MRI is the costliest of all the measurement methods, with steeper costs in equipment, training and maintenance. The next costly system is, doppler ultrasound, although being much cheaper than MRI; finally, PPG and cuff type devices are the least expensive, and usually do not require the same degree of specialized training for the operator as the previous ones. The utilization of more than one type of device or sensor, or even multiple devices of the same type, to obtain a better picture of a specific hemodynamic parameter, is an intricate issue. This is even more important if the devices to be used are of the wireless type, connected through a wireless network (WN); and so, becoming sensor nodes in a distributed network. This paper focuses on the particulars of using multiple, low-cost, non-invasive sensor type devices to monitor hemodynamic parameters from short-to-extended periods of time. Sensor nodal synchronization will be covered and an algorithm to improve the issues with these situations will be presented and discussed, specifically the algorithms' capacity of allowing for the automatic evaluation of cardiovascular markers from multiple sensors without the intervention of a human operator.

The rest of this paper is organized as follows; in section 2 the contribution of this work to general life improvement is framed; in section 3 a review of the relevant literature for synchronization problem is made. Afterwards, in section 4, the proposed solutions are presented. Section 5 presents a discussion of the proposed method; a roadmap of the work being developed and some conclusions for this paper.

2 Contribution to Life Improvement

The methods referred in the previous section for cardiovascular assessment are commonly found in devices that can range from, bulky, with limited portability to simply non-portable (as MRI devices); those can take a variable amount of time to setup for operation and may require a significant degree of training and specialized maintenance. As such, their use in clinical daily practice is of limited use. PPG, oscillometer cuffs and doppler ultrasound devices on the other hand, have been made portable in the last few years and have seen increased utilization in the clinical practice. Currently, doppler ultrasound devices, even in their portable form, require a skilled operator with tens of hours of practice to use the device effectively each time a measurement is taken; PPG and cuffs can, to a significant extent, be set and operated remotely, after the device has been properly placed in the correct position on the patient; the health attendant can be free to perform other tasks. This type of hands-off remote monitoring allows for the patients to be followed over an extended time period and in a more relaxed environment, reducing the white coat effect[1] on the patient's taken measurements [4].

The almost exclusive utilization of any of these types of devices is in a single-channel, single-use form. Currently, in the daily clinical routine setting, only cuff oscillometer type devices are used for 24-hour Ambulatory Monitoring Arterial Pressure (MAPA). Due to the nature of the device setup, the user discomfort can be significative, this being induced by the vascular constriction caused by the measurements at regular intervals – a situation that can become particularly unpleasant during sleep [5]. PPG devices, due to their low cost are now being offered by several vendors and system integrators in several forms. They can be found in smartwatches, as add-on accessories for smartphones or in sport monitoring devices. note that those are only single channel solutions that have, up to now, encountered only very limited clinical utilization.

An innovative device that can use more than one channel for hemodynamic parameter monitoring is a *multi-channel PPG hemodynamic monitoring system*, developed by Portuguese company NMT, S.A. The device can handle several, wearable, sensor nodes that communicate, and are synchronized in a secured distributed WN. The low footprint of the system's sensor nodes along with in-built robustness aims to improve routine clinical practice, freeing doctors and medical staff and allowing for a new degree of freedom of movement and comfort for monitored patients, in and out

[1] The white coat effect or white coat syndrome is a well-documented situation where some people tend to exhibit blood pressure above the normal range in the clinical environment, although this situation doesn't progress out of this setting (i.e. blood pressure readings are normal).

of the clinic. Figure 2 shows the block diagram of NMT's prototype system; currently at technology readiness between level 6 and 7[2] (TRL 6/7).

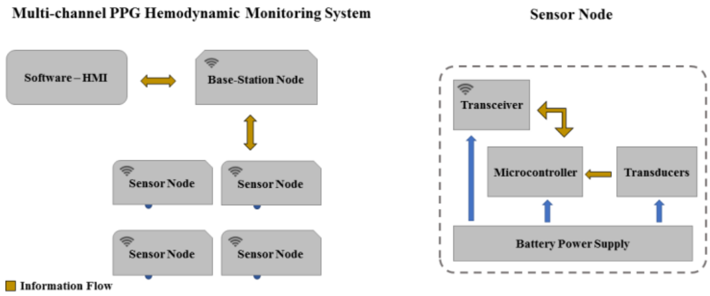

Fig. 2. Block diagram of *NMT, S.A.* multi-channel PPG hemodynamic parameter monitoring system. (Source: author).

3 State of the Art

Using multiple channels and sensors to record physiological markers in the patients the sensor's physical footprint can become an issue. Usually, it's strongly defendant on the type of sensors in use, however, any sensor setup can easily require several different connectors becoming cumbersome, especially if it is hardwired and can´t be used in a more comfortable wearable form. With battery power, wireless operation and reduced footprint, wireless sensor nodes (WSN), can be more user-friendly for the wearer (patient) while maintain the same degree of measurements validity as their wired counterparts; although they can present a series of drawbacks; multi-channel signal analysis and aggregation in a WN can be affected by a number of issues, the most significant ones being synchronization related, additionally, the vulnerability of the sensor channel from outside manipulation should not be overlooked, as a corrupted signal due to external manipulation could lead to a miss-diagnosis and be life-threatening for the patient.

Synchronization of SN in a network has been an area of study for some years now, with initial research being done since the early 2000's and focusing in time-synchronization strategies for multi-nodal sensor networks with several degrees of success and algorithm complexities [6], [7].

3.1 Time Synchronization

In a microcontroller, IC, computer or sensor node, the clock at time *t*, is given by equations (2) and (3):

[2] Technology readiness level (TRL) as defined in: *NASA Systems Engineering Handbook - NASA SP-2016-6105 Rev2* and accepted as a *de facto* industry standard in system development.

$$C(t) = k\int_0^t \omega(\tau)d\tau + C(t_0) \qquad \textbf{(2)}$$

Where, ω is the oscillator's frequency, k is the oscillator related constant and $C(t_0)$ is the time of the tick (click) from the system's implemented hardware oscillator. Where the approximation of the computer time with real time will be given by:

$$C(t) = q * t + b \qquad \textbf{(3)}$$

Where, q is the clock drift and b is the clock offset; ideally $q = 1$ and $b = 0$.

The main reasons that different sensor nodes can present different time clocks can be summarized as follows: *1)* nodes may have been started at different times; *2)* the hardware quartz clocks of the nodes can be running at different frequencies; *3)* the clock frequency can drift or skew due to several factors that can affect the crystal oscillator operation. Variations on the supply voltage, humidity, temperature, pressure and crystal ageing can result in a changing drift rate for the clock (dC/dt-1). More so if for SN implementation is chosen to use off-the-shelve, low cost component modules, (transceiver and such) as they can carry lower quality quartz clocks and other semi-conductor components, that can sum to the drift and skew of the system clock. Additionally, to those situations, events like waking-up, low-energy sleep modes or hardware interrupts can affect normal clock operation, as some clock ticks can be missed for transceiver message handling.

For networked computer-based systems, node protocol synchronization schemes are based on Network Time Protocol (NTP), as implemented in the internet. Where, time server nodes broadcast synchronization packets and each single node performs statistical analysis on the round-trip of the synchronization (sync), packets timestamps to adjust its internal clock's drift. When considering wireless networks and due to the nondeterministic nature of the transmission line (i.e. open air), this type of solution is not feasible; the Medium Access Control (MAC) of radio stack can lead to several milliseconds of delay in each hop exchange, a situation that can be reinforced if a multi-hop strategy is adopted for WSN [6]. Currently, there is no single standard protocol to solve or minimize these issues, but classification for the major topologies is generally accepted in the literature as follows: Unidirectional broadcast, receiver-to-receiver and sender-to-receiver; as shown in Figure 3. The simplest time synchronization protocol type is the unidirectional broadcast type, as implemented by the flooding time synchronization protocol (FTSP); a beacon node with a precision clock broadcast sync signals with a time stamp. this is then used by each WSN to adjust their internal clock drift and jitter [8]. In receiver-to-receiver synchronization a beacon sync message is broadcasted, each SN then exchanges messages with each other to adjust their clock, this scheme type is used in the Reference Broadcast Synchronization (RBS) and adaptive clock synchronization (ACS) protocols [9]. A drawback common to these two types of synchronization methods comes from the limited physical wireless range of the beacon node. Finally, sender-to-receiver synchronization schemes rely on handshake protocols, where the round-trip time of the handshake messages is used by the controller to adjust the clocks and calculate the propagation delay; the scheme is used in Timing-sync Protocol for Sensor Networks (TPSN). Receiver-receiver and sender-receiver protocols suffer an additional delay each time a new SN is added; this is due to the necessity of each SN to exchange sync messages between all the nodes on the same network layer, so growing the network layer beyond a limited number of nodes can bring forth additional delays. The current prototype system is designed to support up to 4 SN, but this number can be easily expanded as necessary in future device iterations.

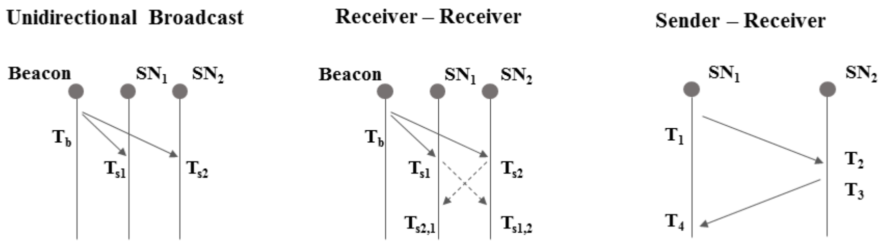

Fig. 3. Classification of the main types of time synchronization topologies.

4 Research Contribution

The implementation of any sync protocol in a practical WSN presents several challenges. Firstly, sensor nodes IC's usually employ low-cost fast drifting clocks, additionally, in some applications, the nodes are battery powered, so an energy conservation strategy to prolong battery life must be adopted. Any single node will spend the maximum possible time in an "off" or "deep-sleep" state. Interrupt, wake-up, settle-time and synchronization times must be considered for operational, "real-world" synchronization schemes. Figure 4 presents the proposed network topology that's under development for this system. The network is divided in 4 depth levels with data communication and node discovery restricted by level and specific node function. Level 0 is the top level of the network and only communicates the HMI-CCV nodes (Human-Machine Interface, Command, Control and Visualization). Level 1 nodes can connect to one or more Level 2 nodes, their main purpose is configuration, setup and visualization of fused signals collected at Level 3 nodes. Level 2 nodes are patient dependent (i.e. 1 per patient is required, at this time) and connect and control the WSN placed on the patient. Per network level, data stream is expected to be done mostly as follows: from Level 1-Level 0, upstream, data with downstream communication mostly for diagnostics assistance results; Level 1-Level 2 communication downstream, done mainly for control and configuration purposes; Level 2-Level 3, here, there has been adopted a hybrid master-slave approach. Fusion nodes (FN), map, synchronize and command the WSN sync'd to them. Any SN can be classified as Level 0, tier 1 node at any given time. A node classified as tier 1 will be considered by the fusion node as the signal acquisition lead; this works in such a way that the sync beacon for all the other nodes will be offset to match the tier 1 clock timestamp. The proposed approach is such that the travel time of the PWV pulse between any node can be precisely synced to get accurate velocities between 2 or more relevant sample points. Sensor signal synchronization is critical at levels 2 and 3 of the network.

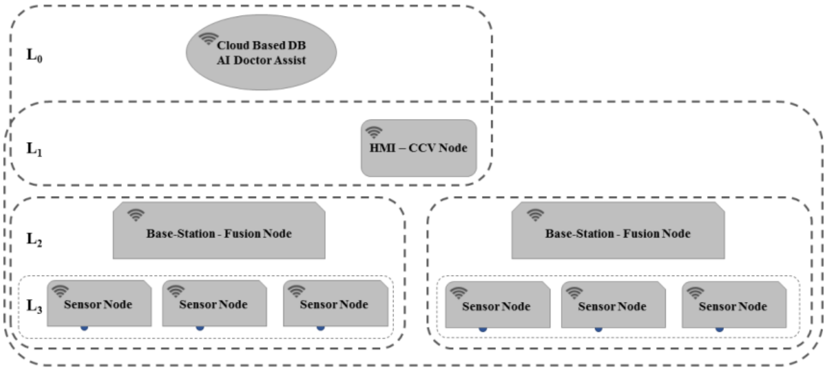

Fig. 4. Proposed network topology of hemodynamic parameter monitoring system with hierarchical levels (0-3).

Due to the nature of the environment in which several FN and SN are placed, they can share the same physical space with nodes going online and offline at random intervals during routine clinical operation as systems are expected to be disconnected after the relevant patient data has been gathered, only to be reconnected in a new patient some minutes later; note that is expected that several patients can share the same space within the network's radio level coverage. Those nodes will typically be unknown to each other and as the radio signal bandwidth must be shared between wireless devices, the MAC layer can potentially be stressed to a point where the number of collisions and message-time broadcast delays can further enhance the sync problem in the WSN, so disconnecting the SN and FN when not in use can be an important advantage under these conditions. As a reference, Figure 5 shows the flow-chart for the fusion sensor at network level 2. Initially, as SN can be interchanged between networks and patients, the mapping of the network should be done at each FN reconnection. Wireless transceivers typically spend more transmission power in the mapping and discovery phase of the network. To minimize power consumption, connection should be done in the best possible conditions. Initial handshake messages can require close to 20ma of current against below 10ma for normal broadcast communication, this for the nRF24AP1 transceiver module (datasheet).

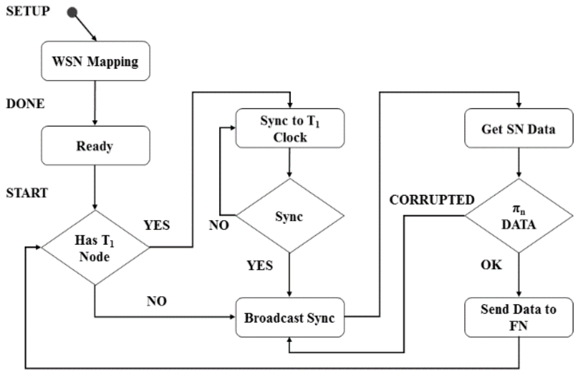

Fig. 5. Flow chart for a network level 2 node, a fusion node.

5 Discussion and Future Work

The proposed synchronization scheme for SN targets working at the lower levels of the network, Levels 3 and 2, is the stage where the data fusion is possible and critical. Most schemes applied to medical devices tend to use multi-channel data analyses as a tool that is used *posteriori*, by qualified personnel, to obtain some conclusions from the gathered data, for this, parts of the signal are selected by the technician for measurement. As it is difficult to guarantee a correct signal synchronization between sample points the result is more times than not, weighted against the technician's experience. The proposed scheme circumvents this reality by matching the measurement at any point on the SN to a single unified time clock, given true, or as much as possible signal integrity across all sensors, thus allowing for automatic signal selection for data analysis, (i.e. automated cardiovascular marker evaluation).

Work will continue in increasing the robustness of the network, especially in cluttered environments, and trying to obtain a greater degree of system automation. The current protocol is not tailored to any specific wireless communication safety standard and so far, only the initial evaluation of embedded security protocols in wireless transceivers has been done. Future work will have to evaluate if those are enough for data safety or if watermarking techniques of messages are necessary for system security.

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