Physio-environmental sensing and live modelling and the role of U-CEP

Extended abstract

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The vision of this paper is to bring together a team of biologists and from medicine regarding the definition of biomarkers with specialists of process or event modelling methodology to implement such biomarkers and with IT specialists of Ubiquitous Complex Event Processing of accordant real-time processing platforms for a tremendous vast amount of events or signals per second. In the final paper we will connect the mathematical approach of Andree Ehresmann and Jean-Paul Vanbremeersch (U Picardie Jules Verne) as well as the approach based on U-CEP and Brain Computer Interface (BCI) as discussed in the paper of Yuri Danilov / Kurt Kaczmarek / Mitchell Tyler (U Madison/TCNL) / Rainer v. Ammon (CITT) / Opher Etzion (IBM)

The interaction of human physiology with environmental conditions is becoming increasingly important to understand the effect of pollution on our health, but also to link lifestyle with the development of health status in general.

Most sectors of modern medicine, handling either prevention or complex intervention, rely deeply on early, accurate, and complete diagnosis followed by close monitoring of the outcomes, also by means of telemedicine/telehealth technologies. To date, this task is carried out by occasional screening of the individual concerned and producing a (time) series of snapshots at biochemical, mechanical, cellular and molecular levels.

From a biological point of view, although very similar, human individuals show a susceptibility to disease that is unique to them. This simple observation has resulted in the concept of personalized medicines or procedures. However, for a personalized treatment to be really effective, we need accurate individualized information obtained at many levels and in a more continuous fashion, sometimes requiring interacting also with the patient’s home environment.

With increasing life expectancy, the number of patients with multimorbidity increases. This complicates diagnosis, prognosis and treatment selection. The traditional medical approach, in which data are collected in a haphazard way, based on inter-current problems regarding a specific diagnosis at the time the patient visit the hospital will not suffice anymore. With increasing life expectancy, the ratio between those who need care and those who provide it, will turn negative. There is an urgent need to shift medical care from institutions to the home environment. More specifically, with the aging of the European population the number of elders and people affected by neurological diseases such as Mild Cognitive Impairment (MCI) or Alzheimer is rapidly increasing. The costs of assistance are also growing and they will soon become unsustainable without changing the way these people are supported. To this end ICT tools are being proposed and studied to improve the support of elderly and disable people while reducing the overall costs of assistance but much more is still expected.

The use of technology platforms allowing to set-up a one-to-many relationship between doctors and patients may be considered as a direct solution for ensuring the necessary quality and intensity of treatment at a sustainable cost. Another required feature of these technological platforms is the quantification of progress related to the subject, which promotes a better modulation of treatment and a faster recovery.

It is clear that this need has to be accomplished using sensitive, respectful, non-invasive approach, which should allow for not interfering with the quality of life and, most important, should be based on the use of affordable and cost-effective solutions.

Much of the world now enjoys unprecedented network speed, high penetration of home broadband and availability of various mobile network options. In this massively interconnected world, where the social network software industries pave the way to massive tracking of personal data and the communication technologies have reached the level of consumer electronics and are virtually ubiquitous, it might be possible to wonder how to exploit such capillary potential information to improve medical systems at large.

The questions are: is it possible to develop new hardware-software technologies capable of sensing simultaneously physiological and environmental signals, for long times, little or not invasively, and with a level of comfort that ensure a wide acceptability? Is it possible to process all these data in real-time with VPH integrative models so as to issue alarms, warnings, or simple recommendations to the subject or to the carers?

In the last decade we have witnessed a rapid surge of interest in sensing and monitoring devices for healthcare and in the use of wearable/wireless devices for a large number of biomedical applications. Also, our environment at home grows more instrumented, interconnected and intelligent [1]. New and more affordable sensor technologies are introducing entirely new monitoring possibilities. Last but not least, in most part of the developing world where a large proportion of global population resides, wireless telecommunication and mobile phones are the definite means of access to quality healthcare [9].

Body sensors technology is now becoming available at accessible price. *Body sensors*[1] are small piece of little or non-invasive equipments that are able to measure biophysical parameters. For example, it is possible to measure the heart beat rate or the body temperature. The possibility to link these data measurement devices with portable communication systems (i.e., smart-phones) is also technically simple. Recent advances in technology are enabling smarter, connected personal healthcare systems that can supply crucial information to significantly improve diagnosis, treatment and condition management.

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1 The first International Workshop on body-sensors was launched in 2004 http://vip.doc.ic.ac.uk/bsn/m196.html while the pHealth conference is already at its 8th edition, http://www.insavalor.fr/phealth2011.

Despite the combined use of the above technologies can provide a synergistic effect in activities related to rehabilitation and personal well being, providing at the same time a support for developing new ways of treatment, this approach has so far found little practical application. The main difficulties in simultaneously using these tools are related to their low integration level; developed by various industrial companies, each device should be provided with a number of enhancements such as monitoring and visualization systems and proprietary software platforms that are a physical barrier to their concurrent use. Furthermore, what is not yet available is a global architecture (or paradigm of data handling at large) for collecting, storing, and using this huge amount of data at a level that can potentially be worldwide.

Especially the processing of data becomes a bottleneck. Nowadays, data are stored in databases and its analysis is mainly done off line. Patients do not directly benefit from information stored in large databases. There will be an urgent need for strong processing algorithms by which it is possible to integrate and translate large amounts of data into meaningful parameters. These processing algorithms need to be based on models of physiopathology with constant updates.

The VPH-related vision in this respect is to provide mathematical models (existing or new) able to use this data in a proactive, possibly automatic, manner (hence the word "live" in the topic's title). Models able to predict the occurrence of a certain event or the emergence of a certain behaviour at the individual or population level (as for example a run-time model checker) would provide an extraordinary instrument for real-time monitoring thus allowing reacting and self-adapting upon an optimised course of action. Analytics programs would monitor device data, collected by sensors and use rules and logic constraints to describe both the environment and the patient health and to compare against targets, track progress against goals, and send alerts when needed (figure 3.1). In this way, health-monitoring solutions also can become more intuitive, comprehensive and affordable.

We already mentioned that the European population is getting older and older. It comes with it that the number of elders and people affected by neurological diseases such as Mild Cognitive Impairment or Alzheimer, as well as by a number of other chronic diseases is rapidly increasing. The costs of assistance are also growing and they will soon become unsustainable without changing the way these people are supported. To this end ICT tools are being proposed and studied to improve the support of elderly and disable people while reducing the overall costs of assistance but much more is still expected.

Examples of areas where sensor-model integrated systems would prove highly useful are: i) monitoring patients with chronic diseases (e.g., Mild Cognitive Impairments, diabetes, epilepsy, chronic cardiac diseases, progressive renal diseases, atherosclerosis); ii) monitoring patients that are hospitalized and need frequent probes; iii) monitoring patient's addiction recovery and long-term drug treatment; iv) monitoring of elderly patients in the daily assessment of generic health conditions. From a developing country perspective, personalized applications might not be economically viable, and prevalent disease pattern differs. But, the same devices and supportive infrastructure can be tweaked for both clinical and laboratory diagnosis at the health facility level [10]. An initiative that is working to innovate in this regard is already in existence[2].

As there is a need of flexible ICT tools for supporting software developing in this new application domain, the synergy between VPH models and the body sensor technology is straightforward. On the one hand sensors will feed realistic data-driven models through the collection of data to be used for model parameter estimation and model result validation in areas where it has traditionally been difficult; on the other hand, models will be able to assess

[2] MoDiSe: http://www.modise.org

the impact on the population, optimize the allocation of resources and devise mitigation and containment measures to reduce economic and (more in general) social disruption. Only through a perfect intertwining of the two components the system will be efficient and efficacious. The whole vision is based on the idea that with more and better information, people can make smarter choices in regard to managing personal health and wellness. As well, this can aid the design of public health interventions; decision-makers can respond quickly to rising disease patterns and intervene smartly, quickly and appropriately.

A crucial feature will be the easiness of use and accessibility to data. In fact, the development of this paradigm of data collection, sharing and health forecast, will strongly depend on how easy will be to share the data and get information back from the available servers.

The building blocks of such health care distributed system span across areas such as mobile devices, home-based devices, web-based resources, electronic health records and personal health records. Hence, its development will involve alliances made up from device makers (electronics industry), healthcare industry, VPH modellers (life science researchers) and ultimately also policy makers to institutionalize the integration of this system in the national health care one. To mention, Continua Alliance[3] efforts in creating a standardized platform for integrating multiple devices for personalised care is worth considering.

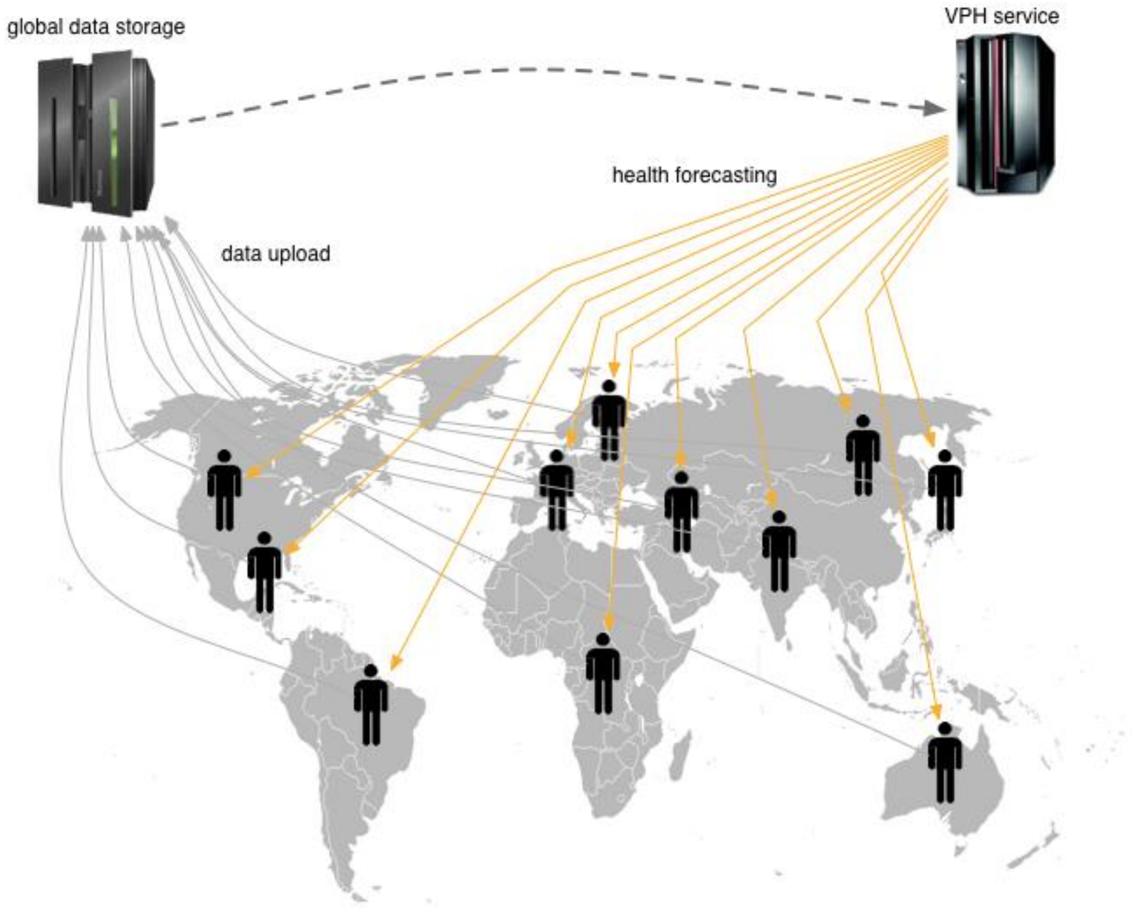

Figure 3.1. *Users upload data via mobile network devices. They get VPH health forecast services through the web or through ad-hoc mobile applications.*

3 http://www.continuaalliance.org/index.html

The challenge

The above vision breaks down to the following key points, each one corresponding to a different research, technological, conceptual and societal challenge.

1. Developing a whole spectrum of wearable sensors. What can be measured cheaply and little or not invasively at all? Developing home-environment sensors that a cheap and wirelessly connected to personal data hubs. Sensors that can communicate seamless with either public and private wireless or mobile networks.
2. Developing a data communication system that is secure and allows partial anonymous retrieval to third parties.
3. Developing a robust storage system that is extensible and upgradable. The data collection needs to be organised by using taxonomies that are well accepted within and beyond the VPH community.
4. Developing information systems (such as web servers or internet resources) exploiting such data. This includes VPH methods and models to provide distilled data or predictions from available information.
5. Developing smart and self-adaptive systems, i.e., intelligent environments for monitoring the human health, regulating the uptake of medicaments and predicting individual emergencies. Developing notice network systems based on overall data able to issue warnings for the population in general.

Body sensors are somehow available nowadays (see the ICT research stream of sensors and wearable devices). However, this area of research is evolving rapidly. Already available sensors include electrochemical, optical, and gravimetric sensors and allow for measurements ranging from the whole body scale (inertial devices for movement measurements) to the body structure level (textile-based devices for biological signal monitoring), to the so-called bioelectric diagnostic chips able to scan bodily fluids for various markers of minor illness and disease[4]. New and most advanced protein-based sensors are especially interesting as environmental pollutants detectors (i.e., sensors based on the folding of proteins, peptides and DNA when they come into contact with compounds of interest).

Moreover, implantable in vivo monitoring devices is a well-developed area of research. It addresses problems such as long-term stability and biocompatibility, system integration, sensor miniaturization, low-power sensor interface circuitry design, wireless telemetric links and signal processing. Apart from technological considerations, a lot of effort in this area of research is devoted to the issue of quality and trust of the service/device. In fact, the level of acceptance of this technology by the users will strongly depend on how reliable - hence useful – is the final output and how well the output is used by the research community to improve our quality of life.

The degree of invasive surgery required to implant such devices will finally depend on the type of user. While chronic patients or elder people are likely to accept anything promising an improvement in quality of life, normal healthy individuals do not. This advocates the first category of citizens as the first to target in leveraging public opinion and policy makers at large.

Smart and self-adaptive systems based on two levels of abstraction, logical and physical, can allow in real-time through long-term trend analysis, prediction, prevention and support of basic daily behavioural and physiological data, building on unobtrusive sensing and advanced reasoning with humans-in-the-loop. The physical level consists of a self-adaptive and self-

[4] http://www.techradar.com/news/computing/cutting-edge-intel-s-bioelectric-wonder-chip-425788

healing middleware that supports the ensemble of adaptive components and their interactive communication within shared contextual information. The logical level provides tools for automatic reasoning enabling the prediction of spatial/temporal object configurations determining dangerous interactions or physiological damages.

The data communication network is already available, since it can rely on common data/voice network technology plus the Internet whereby smart-phones are playing the role of *the* enabling core technology.

For what concerns the area of wireless sensor networks that could provide interesting solutions for the home and pollution detection sensors, it is necessary to develop wireless protocols and to address the problem of its security as well as problems relative to the performance of large distributed systems, fault tolerance and anomaly detection.

What needs to be developed is a bulletproof communication workflow that goes from the individual to the storage facility in an anonymous and secure way. Whereas in principle the data could be stored locally on the device and only later uploaded through a secure connection, in general, embedded systems do not have the possibility to store a large amount of data. Hence the development of secure protocols for run-time measurements upload is required.

Imagine a physician's tool that could evaluate, in minutes or possibly seconds, a wealth of data from connected health devices plus the complete medical history of a patient and all available medical literature (such as medical records, texts, journals, research documents even ongoing clinical trial results), much of which is unstructured information written in natural language. This application could suggest possible diagnoses complete with documented "reasoning" or, alternatively, request additional, seemingly unimportant information needed to test hypotheses.

This idea of tracking progress and stay motivated or to monitor chronic conditions and share data with the personal doctor was the original idea behind Google Health[5] that, unfortunately, has been discontinued (end of 2011) because an unexpected insufficient participation to the project. A similar effort (still operational at the time of this writing) is that of Microsoft HealthVault[6].

For what concerns data standards there exist at least a couple of interesting projects going on. One is the standard for data storage and communication already developed and adopted by both Google Health and Microsoft HealthVault called Continuity of Care Record[7] (CCR), the second is Direct Project launched by the US department of Health and Human Services[8] with the Nationwide Health Information Network initiative in March 2010[9]. NHS Interoperability Toolkit[10] in the UK and HITCH[11] in the EU are also similar ongoing initiatives.

The driving philosophy behind these two efforts is in line with this topic aim. In particular, communication of health information among healthcare organizations, providers, and patients

5 Google Health: http://www.google.com/intl/en-US/health/about/index.html
6 Microsoft HealthVault: http://www.microsoft.com/en-us/healthvault/
7 A standard proposed by the ASTM (ASTM International, formerly known as the American Society for Testing and Materials). http://www.ccrstandard.com/learnabouttheccrstandard. The Continuity of Care Record (CCR) is a core data set of the most relevant administrative, demographic, and clinical information facts about a patient's healthcare, covering one or more healthcare encounters. It provides a means for one healthcare practitioner, system, or setting to aggregate all of the pertinent data about a patient and forward it to another practitioner, system, or setting to support the continuity of care. The primary use case for the CCR is to provide a snapshot in time containing the pertinent clinical, demographic, and administrative data for a specific patient. (Source: http://www.astm.org/Standards/E2369.htm).
8 http://healthit.hhs.gov
9 http://healthit.hhs.gov/portal/server.pt/community/healthit_hhs_gov__nationwide_health_information_network/1142
10 http://www.connectingforhealth.nhs.uk/systemsandservices/interop
11 http://www.hitch-project.eu/about

is traditionally achieved by sending paper through the mail or fax. The development of a standard for data exchange seeks to benefit patients and providers by improving the transport of health information, making it faster, more secure, and less expensive. It will facilitate "direct" communication patterns with an eye toward approaching unprecedented levels of interoperability.

From the VPH point of view, the development of a general storage system consisting in large data-warehouse facilities in charge of providing controlled access to users, does not express a challenge on its own. However, collected data needs to be organised in a strict but also extensible and upgradable manner. This finally comes down to the problem of adopting a standard for names and symbols of biological objects and the use of controlled vocabularies and ontologies to describe repository content. This is instead a VPH (7th Framework Programme) outcome to be opted for and able to foster further development.

Finally on this issue, the aspects connected to the *possibility* to combine data and models in a close synergistic effort to create new information in a way that is both, accessible on the one extreme and secure from malicious usage on the other extreme, is at the same time, stimulating and challenging. Moreover, there are a number of important aspects that should be considered and safely addressed from an ethical point of view. For instance, data from which to derive epidemiological information at the level of geographical regions has an enormous strategic value for industrial sectors as the pharmaceuticals. Data security or integrity is most essential especially if cloud computing is being considered.

Summarising, data needs to be kept private and secure; it should be shareable with health professionals and downloadable for use elsewhere (also accessible through mobile device). Data should be organised according to standardised ontologies and stored in digital formats that are well defined and already adopted.

For what concerns the foundation and development of mathematical and computational methods to achieve prediction and predictability of disease spreading or disorder conditions in our complex techno-social system, this will prompt the development of (new, or the adoption of old) large scale, data driven mathematical and computational models endowed with a high level of realism. VPH models enabled by ubiquitous sensors data will allow the forecast of critical events. Moreover, the design and implementation of original data-collection schemes will be themselves motivated by identified modelling needs. Think for example at the collection of real-time disease incidence data through innovative mobile sensor ICT applications. The set up of computational platforms for disease forecast and data sharing will generate important synergies amongst different research communities and countries.

An unquestionable critical problem is how to drive consumers who lack extreme motivations (such as chronic conditions) to share their personal data. In fact, as already discussed, the system should rely on the participation of the population to collect real-time information on the distribution of biological parameters or diseases by means of their personal body sensors and smart-phone devices (figure 3.2). This is itself a big challenge. How can we reward the individuals to spend their time (and money, since cell data connection is not available for free) and to share personal information with distant entities such as research institutions? Is there a real need to transform this system in an economic model on which to produce revenue, or will the promise to have access to a better health system does the job?

In principle, the potential savings that live modelling and continual monitoring may lead to, through early diagnoses and pre-emptive treatment, may open the possibility of applying novel forms of project financing for innovation. In the same way that many public works programmes across Europe have been financed through a mix of public and private funds in conjunction with the agreement that the private investors would be entitled to a return on their investment through tolls or the equivalent for a sufficient period of time, cost reducing or controlling eHealth innovation may also attract private investment, if a share of the potential reduction in the cost of treating patients can be passed back to the original private investors in the form an "Innovation Dividend". In a contemporary setting, the value of the saving, from which the original private investors would be entitled to a share of, could be derived from the reduction in the average cost (adjusted for inflation) of the care of a sufficiently large number of patients with a specific disease within a region that had been selected to trial the innovation in question for a pre-defined duration. This would result in an economic incentive for innovation that could attract a wide variety of healthcare providers, IT companies and investments institutions, whilst initially stabilising (and later on reducing) the costs of healthcare delivery, management and innovation.

In the future, a product of a fully functioning VPH-based innovative patient- and process-oriented care, based on live sensors-derived model-guided medicine and on consequent model-guided clinical workflows, spanning the entire health continuum from prevention to diagnosis and treatment to rehabilitation and nursing care, will provide scientifically justified health reference costs. As a result of the expected increase in early diagnoses and pre-emptive care, the outcomes of such a system could favourably reflect, in terms of cost, on the contemporary average costs system that was described above, enabling both private investors to benefit from a significant return on their innovation investment and for healthcare providers and patients to benefit from lower costs and higher quality of care. In the long run there is even the possibility that the traditional relationship between income (national or individual) and healthcare expenditure that results in healthcare seeming to be a luxury good could be broken and replaced by a relationship that sees the core costs of healthcare delivery and quality detached from income levels and more closely aligned with innovative solutions to fundamental healthcare needs. Finally, scientifically justified reference costs and evaluated outcomes-oriented management could replace the black-box (hidden, pragmatic) approaches to healthcare systems (including diagnostic, therapeutic, systemic, and managerial) and fully exert a role as potential change drivers.

Another critical issue may be the lag time between data-collection and individual benefit. If meaningful parameters are directly and readily available, this will improve motivation for patient and care givers. Meaningful outcome could be used for online feedback and coaching. Data may be supervised by health workers and be summarized and used as guidance during consultation at health institutions. A constraint of minimal lag time between data import and producing output may put extra demands on data-collection and processing. This perfectly underlines the necessity to develop powerful data processing algorithms, based on physiopathological models that are capable of extracting information at far greater speed than is performed nowadays on static databases.

An inspiring example could be found by looking at the recent societal but also economical phenomena of social networks. These software systems are actually collecting an enormous amount of data without providing any financial reward to individuals. They collect data because people are willing to share information with other people. Note that this is indeed one of the possible reasons for the failure of the GoogleHealth project, as the enthusiasm in sharing personal health data possibly requires the relationship with an institutional partner rather than a software industry. This further suggests that the involvement of institutions in such vision is not optional but rather essential for the successful active support of a critical mass of citizens. The HealthSpace, a personal health record platform operated by the venerable NHS that is also suffering from the same disappointing low utilization, provides a suitable anecdote for reflection[12]. Suggesting that, direct incentives to the patients, citizens or population beyond just an institutional support are required.

[12] https://www.healthspace.nhs.uk/visitor/default.aspx

It is important to show to data providers (i.e., the patients) what the benefits are. On the one hand the system could rely on a kind of “social contract” whereby motivated individuals have a clear return in term of health assistance. On the other hand a business model could be adopted to gain from potential market opportunities. The question is whether a system as the one envisioned will prove to live up to user/patient expectations or the whole solution requires a concrete real market opportunity to exploit. Perhaps the answer lies half way these two extreme in that sensor vendors and communication technology industry can exploit a market opportunity whereas the data exploitation and health forecast although curiosity and research driven will provide enough critical services to boost the interest of a part of the society that is interested and believes in technological advances especially in the health system.

With respect to the data collection, two interconnected points are at the core of the challenge: On one hand, there is how to collect the necessary data, and on the other hand, there is how to ensure that there is not abuse of these data. Both questions need to be handled in unison and robust solutions provided if we actually want to employ this technology. Also, this scenario will be markedly influenced by the growing use of electronic patient records that will be spread in the new few years to all clinical activities.

Finally, besides the technical challenges facing the body-sensor technology (design, biocompatibility, invasiveness, reliability, energy consumption etc.), there are a number of legal, societal and ethical challenges that need to be addressed.

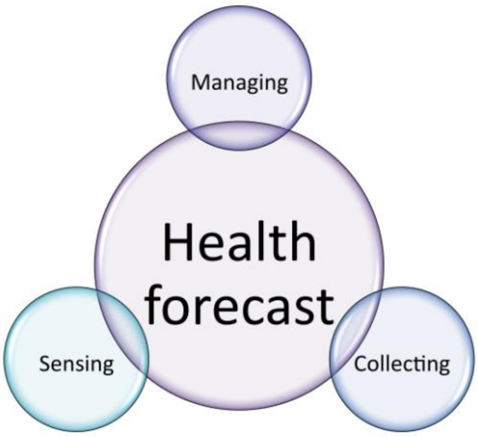

Figure 3.2. *The task of sensing, collecting and managing the data gains a larger significance when combined together with the possibility to produce new and valuable information on the health status of single individuals or entire populations.*

The VPH motivation

Within this context, the expertise accumulated in addressing VPH-type (hence system level) modelling problems by VPH projects has a big value. Hence what VPH will add to the body sensor research agenda is the strong connection between models and data. Data collection must be extended with physiological modelling techniques, which are capable to process the acquired data in real-time and provide individualized warnings and alerts instead of just relying on some simplistic, generic rules.

In this paper we will discuss, how biomarkers would have to be modelled by modelling standards, which artefacts or event types can be used or are missing in modelling standards like BPMN (OMG) or S-(B)PM and which artefacts can be used or are missing in execution standards like (B)PEL or in the execution semantics of BPMN.

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