




An opinion paper on the maintenance of robustness: Towards a multimodal and intergenerational approach using digital twins

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Abstract

The increasing number of frail elderly people in our aging society is becoming problematic: about 11% of community-dwelling older persons are frail and another 42% are pre-frail. Consequently, a major challenge in the coming years will be to test people over the age of 60 years to detect pre-frailty at the earliest stage and to return them to robustness using the targeted interventions that are becoming increasingly available. This challenge requires individual longitudinal monitoring (ILM) or follow-up of community-dwelling older persons using quantitative approaches. This paper briefly describes an effort to tackle this challenge. Extending the detection of the pre-frail stages to other population groups is also suggested. Appropriate algorithms have been used to begin the tracing of faint physiological signals in order to detect transitions from robustness to pre-frailty states and from pre-frailty to frailty states. It is hoped that these studies will allow older adults to receive preventive treatment at the correct institutions and by the appropriate professionals as early as possible, which will prevent loss of autonomy. Altogether, ILM is conceived as an emerging property of databases ("digital twins") and not the reverse. Furthermore, ILM should facilitate a coordinated set of actions by the caregivers, which is a complex challenge in itself. This approach should be gradually extended to all ages, because frailty has no age, as is testified by overwork, burnout, and post-traumatic syndrome.

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1 | THE SCIENTIFIC CONTEXT

1.1 | Maintaining robustness during aging

Robustness has become a crucial issue with the aging of the population.¹⁻³ Living to an age of about 85 years is good news, but beyond the age of 70 years several factors can combine with physiological aging to cause a slow decline. These factors include chronic diseases, but also economic difficulties, widowhood, divorce (a more frequent occurrence than expected after 60 years), loneliness, and depression. For those concerned, this decline inevitably leads to repeated hospitalizations over several years, exhaustion of caregivers (spouses, children, close friends), and eventually placement in a retirement home with death, on average, 3 years afterward. To face these problems as a society, citizens must be encouraged to remain robust as they age in order to prevent loss of their autonomy.

In this context, the definitions of “robustness” and “frailty” are important and have been the subject of much debate.⁴⁻⁶ As a start, the criteria proposed by Lynda Fried^{7,8} are chosen, which fit in with the goal of a longitudinal follow-up on robustness using automated tests at a cost compatible with a large screening policy. Fried’s criteria to measure robustness can be divided into five categories: cognitive function tests, fatigue state, walking ability, muscle strength, and weight. If one or two of these criteria are abnormal, the person is classified as pre-frail; with more than two criteria, the person is classified as frail. The strength of this approach is that it rapidly probes several major physiological functions of the human body, including the central nervous system, the muscular system, but also the digestive system and the metabolism. Indeed, the impact of frailty on intestinal functions (ie, immune response, permeability and absorption, or gut microbiota composition) is as yet mostly unexplored but is certainly of importance.⁹ In particular, even if there is no evidence of a distinct gut microbiota composition in older sarcopenic patients, a recent review concluded that the literature supports the possible presence of a “gut-muscle axis,” whereby gut microbiota may act as a mediator of the effects of nutrition on muscle cells.¹⁰ Hence, nutrition plays an important role within the multifactorial susceptibility to frailty, and the effectiveness of nutritional interventions for its treatment has already been investigated.^{11,12}

Importantly, a pre-frail person can be returned to a robust state. In contrast, a frail state is almost always irreversible.¹³⁻¹⁶ A frail person will almost inevitably evolve toward repeated hospitalization, loss of autonomy and, 5 years later, premature death in nearly 70% of cases. Importantly, frailty is a predictor of morbidity and mortality after major surgery.¹⁷⁻²¹ Frailty is also linked to malnutrition,²² sedentary behaviors,²³ hearing disability,²⁴ hypertension,²⁵ and is associated with social factors.²⁶

In summary, the increase in the number of frail elderly people in this aging society is becoming a major problem: about 11% of community-dwelling older persons are frail and another 42% are pre-frail.^{1-3,14,27,28} Consequently, a major challenge in the coming years will be to test people over the age of 60 years to detect pre-frailty at the earliest stage and to return them to robustness using the

targeted interventions that are becoming increasingly available.²⁹⁻³¹ This challenge requires individual longitudinal follow-up (ILF) or monitoring of community-dwelling older persons using quantitative approaches. This paper briefly describes an effort to tackle this challenge. Extending the detection of the pre-frail stages to other population groups is also suggested.

1.2 | Maintaining robustness is a problem at any age

Little is known about how humans can adapt to the rigorous environmental requirements that have been created over the past 150 years. These new types of environment are complex in the sense that they are radically different to the environments of the last 7 million years, which have shaped the human central nervous system since the appearance of bipedalism. In this context, one is entitled to ask, can it be said that the human brain is indefinitely adapted and adaptable to human-generated environments? In other words, why would a completely artificial environment created by a biological organism be necessarily compatible with the same organism’s functioning? For example, does this adaptation guarantee that persons with chronic diseases and handicaps can live an independent and satisfying life in a complex urban environment? More generally, are these artificial environments compatible with sensory or motor disabilities, regardless of the person’s age? Also, increasingly intelligent machines are continuously being built, so what are the guarantees that operators will continue to be capable of driving them? This list is not an exhaustive list of the questions that require answers.

Therefore, long-term monitoring should take place of human groups that are engaged in complex behavioral tasks, and this includes seniors. It is proposed that these groups be named “high-maintenance cohorts (HMCs).” They must be monitored to evaluate their training and, once trained, regular verification that their skills are operational should take place. HMCs should also be monitored to ensure they are not exposed to excessive stresses that could lead to depression, overwork, overtraining, burnout, or post-traumatic syndrome, which are prevalent in current society. Following this definition, it is clear that HMCs are diverse, and given the evolution of society, their number will inevitably increase. To quote a few examples, HMCs include not only seniors, but also persons of any age with chronic diseases, handicaps, those in rehabilitation, operators of complex human-machine interfaces, military personnel on active duty, high-level athletes, and so forth. It is believed that the concepts of pre-frailty and frailty are useful for monitoring many types of HMCs, with little adaptation from the original HMC definition.

1.3 | How might we monitor HMCs over the long term?

It is theoretically feasible to use population screening tests to establish a healthy aging trajectory and maintain robustness.^{32,33} However, as

indicated by the review of Rodriguez-Laso et al,³⁴ there is still little evidence for the effectiveness of population-level screening, monitoring, and surveillance of pre-frail and frail people. In particular, the development and evaluation of community-based programs is needed, including a quantitative approach based on electronic health records and an adequate set of sensors. This group has been pushing to achieve this for the past 6 years by taking advantage of a series of developments around 2007, including the introduction of the iPhone, development of the video game industry, the Internet of Things (IOT), and Moore's law, which have led to an epistemological revolution. For the first time, sensors that are noninvasive or minimally invasive and are, above all, inexpensive have allowed "in-the-field" human behavior over time and under "ecological" conditions to be precisely quantified. At the same time, the emergence of equally inexpensive techniques has allowed for characterization of the biological and psychological profiles of a large number of individuals who could also be genotyped at reasonable cost. The combination of these advances has paved the way for overall evidence-based medicine and particularly the early detection of pre-frailty and frailty. Also, new perspectives for the study of human-machine interfaces and quantification of human behavior in the field (war zones, sports stadiums, etc) have opened up.

Our research group has been active in these research fields, which has led us, along with others, to (re)discover and quantify two major characteristics of human behavior. On the one hand, human groups that are supposedly reasonably homogeneous (for example, stroke patients and airplane pilots, who have been investigated by the current authors) turned out to be extremely polymorphic, with large interindividual variability. On the other hand, the behavior of these people at an individual level tends to be surprisingly stable over time. Several studies undertaken to explore the feasibility of building and mining databases that have been used to implement the ILM of normal and diseased humans will be briefly summarized below. For the reader interested in more details, please refer to some more recent publications on the topic.³⁵⁻⁴¹ These studies have confirmed two well-known hypotheses and have opened up a series of questions:

- Detecting pre-frailty and frailty at an early stage, in clinics, companies, sports stadiums, and war zones, and so forth, should indeed be based on ILM and personalized treatment. In short, "tailor-made" solutions are created for each person.
- The construction and mining of large databases that bring together behavioral, biological, psychological, economical, and sociological variables collected during ILM will be the key to "maintenance" of an individual as a biological and cognitive machine. These databases will allow for the detection of pre-frailty, and hence allow the prevention of frailty to be maximized.
- The construction and mining of these databases for human behavior will provide important political and economic leverage. Hence, the following questions are already arising: Who should control this process: the public sector, the private sector, or both? How can data confidentiality be controlled? What ethical rules should be enforced? How might we tackle the risks surrounding

the right of access to personal raw data?

1.4 | Digital twins and predictive maintenance

After stating the approach for monitoring of HMCs, it is clear that this approach is reminiscent of two emerging concepts in industry: digital twins and predictive maintenance.

A digital twin is a digital replica of a living or non-living physical entity. By bridging the physical and virtual worlds, data are transmitted seamlessly, which allows the virtual entity to exist simultaneously with the physical entity. "Digital twin" refers to a digital replica of potential and actual physical assets, processes, people, places, systems, and devices that can be used for various purposes.⁴² Digital twins integrate the IOT, artificial intelligence, machine learning, and software analytics to create living digital simulation models that update and change as their physical counterparts change. In summary, a digital twin continuously learns and updates itself based on multiple sources in order to represent its near real-time status, working condition, or position.

Predictive maintenance evaluates the condition of equipment by performing periodic (offline) or continuous (online) equipment monitoring. The ultimate goal of the approach is to perform maintenance at a scheduled point in time when the maintenance activity is most cost-effective and before the equipment loses performance within a given threshold. Clearly, digital twins will take predictive maintenance to the next level.

It is hoped that these definitions speak for themselves in explaining why these two concepts could help in the monitoring of HMCs, despite the fact that neither of them have yet been used for human monitoring. First, it is believed that these concepts can be a source of inspiration, because similar tools (IOT, database mining) and concepts (digital replica, machine learning) will also be at work for the maintenance of the robustness of the human biological machine. Second, this paves the way for the adaptation of hardware, software, and mathematical models dedicated to digital twins and predictive maintenance in industry for monitoring of HMCs at reasonable cost, and for the cost to be gradually reduced.

2 | METHODOLOGICAL APPROACH TO MAINTAINING ROBUSTNESS

2.1 | Objectives

Maintaining robustness of HMCs required three objectives to be fulfilled. The first objective was to quantify their behavior by making measurements in real time and at the correct sampling frequencies. Most importantly, the measurements were noninvasive, or at least minimally invasive. That is, the individuals being monitored were able to continue their in-the-field activities. This was basically an engineering problem and in some cases it was successfully solved

(see below). The second objective was to enrich these behavioral databases with a variety of data. This included the evolution of several biological variables during the observation period. Indeed, translational research is beginning to focus on understanding the biological mechanisms of frailty by identifying potential biomarkers of the condition,^{43,44} investigating targets for treatment, and developing novel pharmacological drugs targeted at the endocrine components of frailty.⁴⁵⁻⁴⁸ Other variables of interest include psychological (responses to questionnaires), neurocognitive (batteries of tests), and sociological variables; and the genotype. Also, data can be extracted from GPS, presence detectors, pressure sensors, smart water, gas and electricity meters, and so forth. This is an ongoing study. The third objective underway is to merge these composite databases for the benefit of HMCs. In particular, a complex problem was to determine intra- and interindividual standards for statistical bases in order to understand the fine lines between physiological and pathological states, and reversible and non-reversible states. For instance, it was necessary to be able to predict the risk of falls for persons that had never fallen before. In brief, maintaining robustness requires multidisciplinary teams working together from the outset.

2.2 | Guidelines

Several guidelines have emerged over the course of this study that have turned out to facilitate ILM. Obviously, data collection should not be an intrusive or burdening experience for the persons involved. Concerning the first point, the use of cameras was avoided in hospitals and homes. Ethical rules (the General Data Protection Regulation in Europe) were strictly respected. The choice was also made to aggregate the data in the electronic medical record of the person under scrutiny, which solved problems concerning data ownership and confidentiality. Also, it was important that the aggregated data were raw data, and were indexed by specialists. This became problematic over the years because of an increasing number of biomedical recorders that do not allow access to this raw data. Once the data were recorded, reliable and useful information must have been provided to the persons and those surrounding them (doctors, coaches, social workers, senior staff, etc) almost instantaneously. This was essential if the data collection was to be experienced as a fruitful exchange.

Being monitored should not be cumbersome for the subjects due to the installation of IFL on a long-term basis. Until recently, this seemed utopian, but it has become progressively easier to implement IFL with the development of pervasive (or even ubiquitous) computing. In short, the sensors, data collection from the sensors, pre-processing of the recorded information, and transmission to databases can now be integrated into utensils, furniture, doctor's consultation room instruments, athlete's training room tools, and so forth. Unlike a personal computer, which is used for a single activity and for a specific purpose, a ubiquitous computing user interacts with several sensors and actuator systems simultaneously during his/her routine

activities. At best, the user becomes unaware of data recordings because the human-machine interaction is unnoticed.

Finally, it should be stressed that ILM is a tool and that cohort studies of HMCs are essential to generalize and validate what ILM can uncover. That is, the collection of thousands of ILMs is required to establish some sort of taxonomy of trajectories, a limited number of prototypic behaviors and their evolution, whether concerned with the detection of pre-frailty, sports training or monitoring of complex man-machine interfaces, and so forth. Obviously, this poses the problem of scaling up ILMs, which is the present goal.

3 | DETECTION OF PRE-FRAILTY AND FRAILTY BY INTEGRATION OF SENSORS AND ACTUATORS

Over the past 5 years, sensors and actuators have been combined in different ways depending on the objectives of the planned studies. Details will not be given here on the studies currently being conducted (eg, a study with Thales on the cockpit of the future using aircraft simulators; or a study in conjunction with the French Federation of Rugby on collective intelligence using a robot that simulates the "ruck" in rugby^{40,41}). The focus here will be on devices that seek to prevent frailty.

Four types of clinical devices at different degrees of completion are being tested in the Ile de la Réunion and in various clinical departments in Paris. These devices use a common capturing method with adequate physiological features but the environments are different. Then the devices upload the locally encoded data to a "Cloud" where algorithms quantitatively assess robustness and detect frailty and pre-frailty. Finally, the processed data are returned to the user in a matter of seconds.

3.1 | Smart Check

Smart Check aims to automatically measure the five criteria of Fried^{7,8} to assess the degree of robustness of a person in consultation and in the field. It is a portable device that includes a tablet, various questionnaires, five inertial motion units (IMUs), a force platform, a grip pressure sensor, a reference database, and dedicated algorithms hosted on a Cloud server. Smart Check allows the user to obtain a weight measurement, multiple features concerning static equilibrium with eyes closed and eyes open, locomotion, U-turn, head movement, grip force, the sense of fatigue, and an approximate measurement of cognitive function using questionnaires.

On paper, the concept was simple. Considerable progress in sensor technology, the IOT, and the construction and processing of databases allows ILM of the robustness to be performed for each individual from age 60 years onward. In practice, this project was more complex and "delicate" than expected: including the design and industrial implementation of a system capable of rigorously quantifying the criteria defined by Fried, but also having an in-field implementation for non-medical

staff. It took 5 years for a multidisciplinary team that included neurophysiologists, physicians, computer scientists, and engineers to produce the first operational industrial version of Smart Check at the beginning of 2019. This means that it is finally possible to test the robustness of several thousand people effectively, ergonomically, economically, and repeatedly, and thus detect the first signs of frailty (ie, pre-frailty), provided that sufficient financial resources are in place. Screening can and should be implemented by non-medical staff outside the hospital. Eight patients have resulted from this study, along with as many publications, and it is now possible to detect whether a person is at risk of falling before a fall occurs.

3.2 | Smart Flat

Until now, the precise quantitative description of normal and pathological human behavior has involved the use of complex equipment located in laboratory structures and sometimes in hospitals. Therefore, quantitative ILM of human behavior has not yet been analyzed over many weeks. However, the recent appearance of Smart Homes or, more modestly, Smart Flats, opens new possibilities. A Smart Flat is usually defined as a residence that has security, air conditioning, appliances, TVs, lighting, heating, computers, audio and video systems, camera systems, and so forth that can communicate with one another and with remote servers and can be controlled remotely by clocks, from any room in the home, and remotely from outside by phone or internet. These smart devices facilitate the life of the occupants and allow savings to be made. In this context, this research group has worked during the past 4 years to assemble smart devices that can be retrofitted to homes of single community-dwelling adults to monitor their status online in terms of robustness. However, these intelligent habitats, which allow normal and pathological human behavior in “ecological” situations to be quantified, can have a diverse nature: they may be individual houses or apartments, rooms in retirement homes, clinical observation apartments in a hospital, or confined habitats, such as a submarine or a space station.

This research group is trying to design three types of habitat: a clinical observation apartment in a hospital, several flats in a medicalized residence, and several homes for sole community-dwelling seniors. The objective is to keep the occupants of these habitats in a robust state by early detection of signs pointing to transitions from a robust to a pre-frail state, and from a pre-frail state to a frail state. These habitats generate indirect and reduced measures compared with what can be achieved with Smart Check. However, the data can be collected for multiple weeks and are sufficiently precise to trigger an intervention by the person's entourage and/or health-care team. Concretely speaking, the current Smart Flat prototype offers basic equipment that includes on/off radars to calculate the person's mobility at home, pressure sensors on a seat to quantify the “sit to stand test,” handles equipped for measuring grip force, door opening and closing sensors, and a connected scale that measures the person's weight and static balance. A mirror is also being developed that is capable of analyzing the person's facial expression online, along with

a screen to ensure communication with the family, caregivers, and support team (see Smart Com below). The Smart Flat for isolated seniors will be industrialized in 2020, and its first prototypes are currently being tested on the Ile de la Réunion.

3.3 | Smart App

Smart App is a prototype that is currently under development and testing. This app is a further derivative of Smart Check, which is aimed at monitoring heart rate, navigation, and postural and motor control of ambulatory people. Again, the concept is to collect data to detect a transition from the robust to the pre-frail state. This prototype of the Smart App involves GPS, a heart rate monitor, and one or more IMUs depending on the purpose: a single belt accelerometer for simple screening; or accelerometers for the legs and arms, or even the head, to allow more in-depth testing of the patient's locomotor system. The presence of GPS allows for assessment of the individual's navigation skills. For example, excessively long duration for a daily walk to the bakery, which is found using the GPS and IMU signals, will lead to suspected lameness or depression. Erratic routes may point to early signs of Alzheimer's disease. Smart App is above all a warning system.

3.4 | Smart Communication (Smart Com)

Fried's criteria cover several major physiological systems. However, the aging process also involves social, emotional, economic, and professional dimensions. Economic wealth, the quality of housing, a person's greater or lesser loneliness, and so forth also play a decisive role in maintaining a robust state.^{26,49} However, Smart Check or Smart Flat do not explicitly take these factors into account. Smart Com is under development and aims to provide a first response to this problem. Smart Com is an interactive digital screen that will allow for a great deal of qualitative data to be collected and the subjective frailty of the individual to be assessed via regular online dialogs with the family, psychologist, social workers, and so forth. Considering that feelings of loneliness increase the risk of depression and anxiety and therefore the risk of frailty, Smart Com also aims at facilitating the socialization and the connection of the patient with the family and residential, associative, and medical environments.

4 | CONCLUSION

These projects focus on collecting quantitative sensorimotor, cognitive, and psychological data to assess frailty. Later genetic and biological data for community-dwelling seniors or HMCs will be collected. It is progressively being learned how to monitor individuals at home and in outpatient clinics, intermediate housing, retirement homes, hospitals, and so forth. To implement ILM, databases have been built and mined in order to quantify normal and

pathological human behavior. With appropriate algorithms, faint physiological signals can begin to detect transitions from robustness to pre-frailty states and from pre-frailty to frailty states. It is hoped that these studies will allow older adults to promptly receive preventive treatment at the right institution and from the correct professional in order to prevent loss of autonomy. Altogether, ILM is conceived in the same way as shown in the emerging study of database properties (ie, to be a digital twin). Furthermore, ILM should facilitate coordinated action of the caregivers (ie, analogous to predictive maintenance), which is a complex challenge in itself. This approach, which has been initiated among community-dwelling seniors, should be gradually extended to all ages, because frailty has no age in this complex society, as is testified by overwork, burnout, and post-traumatic syndrome.

Building and mining appropriate databases for ILM requires multidisciplinary teams, which brings together several types of health professionals, neurophysiologists, engineers, and mathematicians, and results in the development of a preventive health policy. Also, these projects call for further development of noninvasive sensors to more accurately capture physiological data. Finally, large-scale implementation of a predictive and preventive policy to maintain robustness will require a win-win public-private partnership to defend a solidarity-based health policy. Alternatives based on a more commercial approach exist but are not the favored option by this research group.

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CONFLICTS OF INTEREST

Nothing to disclose.

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