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Review Article

Unraveling Health as a Complex Adaptive System: Data Mining, Cloud Computing, Machine Learning and Biosensors as Synergistic Technologies

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Introduction

The multiple variables that encompass human health range from microbial and viral vectors, through organismic biological and psychological processes to socio-cultural and other environmental factors. While dramatic improvements in health have been achieved by technical interventions as simple as John Snow's removing the pump handle from London's Broad Street well which was contaminated with cholera (public health) and the advent of antibiotics which successfully treated many infectious conditions (allopathic medicine), technology is becoming increasingly complex, sophisticated and omnipresent. For example, the so called"Internet of Things" may not apply just to "Smart Homes" and other commercial consumer goods, but may facilitate the reality of "Smart Health" as a public utility. Using the framework of complex adaptive systems analysis[1], approaches such as data mining and visualization, cloud computing, genomic analysis and modification, machine learning, artificial intelligence and microelectronic bio-monitoring have fostered an increasingly powerful synergistic ability to understand and improve human health.

Methodologies

While the understandable major concern of most individuals is their own health status and that of their primary support network, understanding of population health and its dynamics are essential to informed policy development and practice guidelines. This paper will describe the synthetic amalgamation of techniques that will both greatly improve clinical practice with individuals and provide a powerful methodology for monitoring and modulating population health. The constituent technology elements will be described and two exemplars of this approach will illustrate its functionality. Other recent studies that illustrate the potential value of such an approach will be described. While this approach was described in more generic terms as a "Perfect Storm" in our understanding of human health [2], further technological infrastructure has been developed that demonstrate the feasibility of this conceptual approach. The model described by the National Institute of Standards and Technology as the Analysis as a Service (AaaS) [3] has been developed and exemplified by IBM's Watson Analytics (WA) [4], which is a cloud based AaaS that can carry out a number of significant data analysis and display approaches in a user-friendly manner(Figure 1). The Explore and Predict modalities use a variety of data clustering and machine learning approaches that can go far beyond single variable linear prediction, while the Assemble modality develops effective data display and infographics.

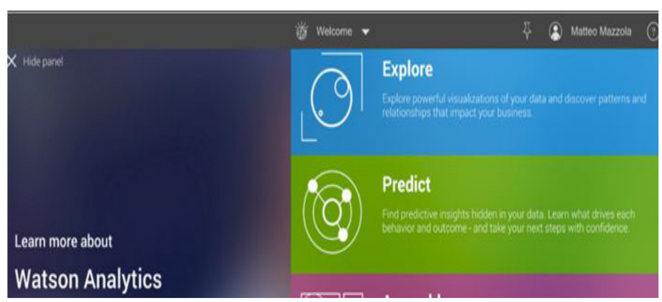

Figure 1: Watson Analytics (WA) Home Screen Showing Three Modalities: Explore, Predict and Assemble.

The first exemplar to be presented is based on the work of [5] to demonstrate proof of concept for a cloud based data acquisition and analysis system which can make accurate clinical diagnostic decisions differentiating patients with Heart Failure from normal individuals on the basis of Heart Rate Variability (HRV). HRV is the extent that heart rate varies over time and has been studied extensively [6]. HRV was first identified as a robust predictor of sudden cardiac death, but is a health biomarker regarding many physical diseases and psychosocial conditions and functions [2]. As illustrated in (Figure 2), the process involves data acquisition using the Physio Bank and Physio Net[7]to obtain and categorize

ECG data into the appropriate format of R to R intervals using the Physio Net HRV Toolkit. This data consisted of 15 subjects with severe heart failure, 29 subjects with moderate heart failure and 54 healthy subjects with normal respiratory sinus arrhythmia. All subject data was collected using standard ECG protocols (8 lead). The resulting data set was examined by WA and a variety of commonly used HRV statistics were derived. These statistics were compared to the data available in the current literature. (Figure 3) shows the results concerning accuracy of prediction using the Total Power HRV (TOT_PWR) statistic with a 90% predictive accuracy.

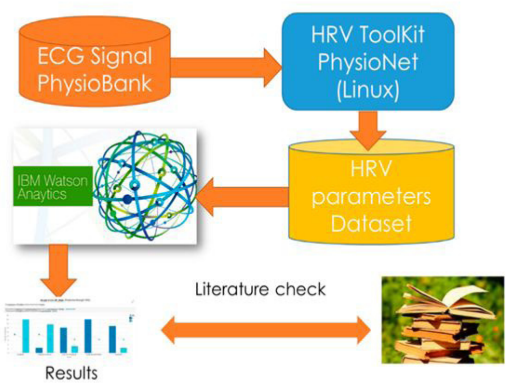

Figure 2: Diagram showing the Guidi et al. Study Workflow.

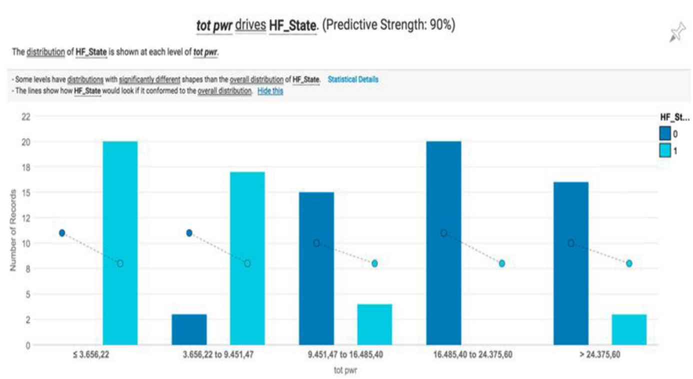

Figure 3: Results for Long Term Hearth Rate Variability (HRV), using TOT_PWR as Single Predictor in the Guidi, et al. study.

While the work of Guidi, et al. demonstrates the viability of the method of data analysis using WA cloud computing with a high level of predictive accuracy, the second exemplar is the work of [8], who studied actual trauma victims who were being remotely triaged for possible helicopter evacuation using simple R to R interval HRV data obtained at the trauma site. This study was in the decision support tradition comparing field recommendations made by on scene paramedics and ambulance attendants versus the use of a brief 4 minute HRV sample obtained on the scene on a Mars Holter monitor sampling at a rate of 128 samples per second. This produced over 2,300,000 data points, completely adequate for analysis. The data collected on 75 subjects showed the simple HRV measure SDNN (standard deviation of non-normal intervals) to be a superior predictor compared to routine trauma criteria or en-route pre-hospital vital signs. The sensitivity, specificity, positive predictive value, and negative predictive value were 80%, 75%, 33%, 96%, respectively, with and an overall accuracy of 76% for predicting a life-saving intervention in the emergency room, such as airway clearing, breathing regularization, and hemodynamic stabilization [9]. While this study was retrospective in that the HRV SDNN predictor was not used in patient care, it is clearly suggestive of the crucial role such remote data acquisition and analysis can play when wedded to the high throughput analytic processing currently available through WA and other AaaS systems. King et al demonstrated a clinical triage application which improved accuracy of life saving interventions, but a wide variety of other clinical applications could benefit from that approach, including the detection of heart failure using HRV as in the Guidi study. Review of the rapidly growing HRV literature [2] reveals that many physical and psycho-social conditions and disorders are related to impaired HRV and in some cases, such as septicemia, can detect occurrence of disorders before the patient has any subjective awareness (symptoms) of the disorder, making prompt diagnosis and intervention possible.

In the difficult task of exploring complex relationships that effect health status and outcomes, Davidson and colleagues at Wisconsin (2005) [10] combined fMRI assessment of CNS and cardiac functioning to elucidate the central pathways involved in response to threat evoked by electric shock. Although it is currently acknowledged that there is a bidirectional causal linkage between the CNS and the heart, this study did not utilize HRV and brain stem fMRI to explore the role of the vagus nerve in modulating this relationship, described by Porges in his Polyvagal Theory [6]. This relationship between CNS and cardiac function was further explored by Walker and colleagues at Berkeley (2015) [11] noting the modulating role of sleep deprivation in impairing the central and peripheral neural discrimination of social threat. In both studies, advanced neurophysiological data was collected but powerful AaaS methods were not used. Clearly, such methods may yield significantly improved understanding of mechanisms of health and well-being and avenues of intervention.The advancement of technology is not only facilitating sophisticated applications such as data mining, cloud computing and machine learning, but driving progress in miniaturized wireless electronic data acquisition systems capable of collecting a wide variety of parameters. Not only is HRV data based on heart rate relatively easy to collect and transmit for processing via Bluetooth, but measures such as activity level measured by accelerometers and respiration data can be routinely gathered in real time. (Figure 4) shows a miniature device and three parameters being gathered from a volunteer subject in conditions of rest, exercise and recovery, which are transmitted to a laptop computer for demonstration purposes [12].

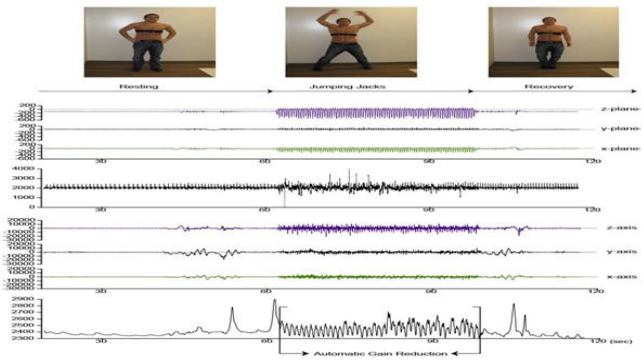

Figure 4: Demonstrating the Use of a Wireless Multi Parameter Biosensor in Conditions of Rest, Exercise and Recovery which was Transmitted in Real Time to a Laptop Computer via Bluetooth.

Discussion

The importance of improving the quality and safety of individual clinical care is clear, but a potentially even more powerful application of the proposed synthetic system of wireless biosensors for unobtrusive data acquisition and cloud based AaaS analytic processes such as WA, is to conduct population health research which can prospectively carryout epidemiological studies, including in real time if desired. Because HRV is a psychobiological signal not requiring subjective report by the patient, it may both simplify and increase the objectivity of important inquiries into the determinants of not only health status and well-being, but more optimal and positive functions such as the observed finding that HRV measures executive functioning by Thayer's group [13]. While these prospects are exciting, there are, of course, problems to be overcome in the application of any technological innovations. Interruptions of cloud computing platforms can be not only inconvenient, but costly in business ventures and possibly dangerous in medical and health settings. While the value of some measures of HRV such as SDNN have been demonstrated, there are a number of promising HRV statistics, both linear and non-linear, that may prove more valuable, especially since non-linear functions are more characteristic of living organisms than the linear relations frequently found in machines and other inorganic phenomena. A major concern with the utility of any health biomarker is of course, its specificity, how accurately it indicates the presence of a specific pathological condition. While extremely sensitive, HRV at this point is not highly specific, but this does not mean it has no value. For example, in studying the putative relationship between autism and cancer [14], the following graphic in Figure 5 shows the pattern of complex relationships that exist between the two clinical entities. Although these relationships have not been well described, they clearly are helping develop a greater understanding of the two important categories of pathology. Likewise, HRV has been shown to be associated with the incidence and severity of many pathologicalconditions and psychobiological functions, although much additional work is necessary to clarify such associations to the maximum benefit.

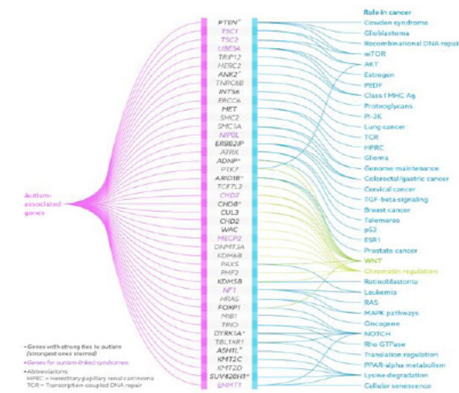

Figure 5: Shows Associations Autism Related Genes and Cancer Constituents [14].

Conclusions

The health care system in the United States is in a state of chaotic disarray and dysfunction. A major contributor to the crisis in health care is the multidimensional nature of the variables involved, which runs from the microbial and bacterial to include organismic variables in the psychobiological makeup of human beings and includes institutional, political and social structural variables such as government regulatory strategies and the practices of corporate entities, such as pharmaceutical and insurance companies, as well as other advocacy and special interest groups. The most promising direction forward in healthcare and well-being is an approach that is integral, personalized, prescriptive, participatory, and practical. Hence,iP.4 Health [6]. This article has reviewed a proposed synthesis of several emerging technologies that can potentially contribute in that arena, specifically, a useful, practical and inexpensive measure of health status and outcome that possesses functionalities in both clinical and population health assessment and intervention.HRV is offered as a methodological example which has successfully been demonstrated in proof of concept and is ready to be integrated into a systems approach using WA, an AaaS approach. While far from addressing all the multifarious issues identified, above, this wedding of appropriate technology may help catalyze progress to the extent that science-based information is valued. Of course, such a venture is still in the early development stage, but the concept has been proven and demonstrated and awaits the applications of appropriate resources to advance to operational capability.

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