Moving Medical Semeiotics to the Digital Realm

SEMEOTICONS Approach to Face Signs of Cardiometabolic Risk

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Abstract: In modern medicine signs derivable from face observation remain an important part of the physical examination that, together with the anamnesis, constitutes the basis for a rational decision-making. Therefore, face semiotics may be considered as a potential source of information for obtaining markers of obesity, metabolomics, cardiovascular homeostasis and psychophysical status. Once properly mapped to computational descriptors, their systematic exploitation is expected allowing the building of effective self-monitoring systems. In this perspective, in the frame of the FP7 project SEMEOTICONS, the most relevant face signs of cardio-metabolic risk are reviewed and analysed so as to drive their detection, quantification and integration into a virtual individual model useful for cardio-metabolic risk prevention.

1 INTRODUCTION

Human face has been always considered to be a mirror of emotions, mood and health status. Face signs have been studied since the time of Aristotle. Hippocrates already described aspects of pathological conditions related to face, becoming common heritage to associate face traits with character, psychological dispositions and health status.

In present days, medical semeiotics deems the face as an important revelaer of precious information about the healthy or unhealthy status of individuals, produced by the combination of biophysical signs and expressive features. Experienced medical doctors acquire a personal and typical ability in reading and interpreting the complex and composite signs of patients' face. These signs usually suggest how to steer the medical examination and may contribute to suggest which diagnostic investigations are to be prescribed. So far, although its striking importance, semeiotic evaluation has not raised a systematic scientific interest. Despite the face represent a naturally pre-eminent mean for communication among human beings and modulating inter-personal interaction, the valuable pieces of information conveyed by human face have not been comprehensively investigated with the aim to assist medical professional and individuals with computational tools.

Nowadays, results from clinical and epidemiological studies strongly stimulate the development of personalized health care systems. This is also in view of new and more efficient strategies for disease prevention, which is a strategic objective for modern health systems. On the other hand, personalized systems working at individual home offer a significant way to contain health care costs with improved effectiveness and efficiency.

Proficient self-monitoring coupled to individual education and coaching is key point to build systems capable to help people staying healthy. The FP7 project SEMEOTICONS (SEMEiotic Oriented Technology for Individual's CardiOmetabolic risk self-assessmeNt and Self-monitoring) has as a major technological objective the building of a multisensory system having the appearance of a conventional mirror, called the *Wize Mirror*, to be hosted in everyday life environments (including individuals' home, pharmacies, fitness centres and schools). The *Wize Mirror* will exploit face semeiotics to instantiate a Virtual Individual Model (Honka et al., 2011) from which a Well-Being Index (WBI) will be obtained. Starting form an initially defined state, tracking WBI temporal evolution will enable individual to self-monitor life-style related

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risks for cardio-metabolic diseases and implement personalized prevention actions.

In the following, we will review and analyse some basic aspects of face semeiotics so as to define the traits of a related computational model.

2 MEDICAL SEMEIOTICS

The face is a fine descriptor of a person's well-being state and, people, not only doctors, commonly derive from the observation of the face significant clues about psychophysical condition. Evidence on the state of nutrition, fitness, and mental state can be obtained. In addition, conditions affecting the colour or the appearance of the skin can be also revealed.

The appearance and features of the face allow the distinction among ethnicity, gender, age and emotions (such as happiness, sadness, fear, anxiety, and pain). Face changes can be due to alterations of skeletal and/or muscular structure, subcutaneous tissue, colour of the skin and eyeballs appearance. For examples, chronic endocrinological diseases (achondroplasia, acromegaly) and congenital anemia (thalassemia) may produce characteristic alterations of bone structures. Diseases of the nervous system (Parkinson, myasthenia, tetanus) may cause typical variations of the muscular structures. Other local and systemic illness may induce modifications of the superficial tissues due to changes of water content, growth of adipose tissue, and deposition of mucoproteins such as in the case of myxoedema (hypothyroidism). Haemoglobin concentration, oxygen saturation, vasodilation or vasoconstriction affects the colour of facial skin (pallor, redness, and cyanosis); moreover the deposit of other substances may be responsible of pathologic appearance of the skin, as bilirubin in jaundice. Local accumulation of cholesterol may become evident with the appearance of xanthelasmas in the eyelid and arcus cornealis, a white ring in front of the periphery of the iris. Moreover some clusters of characteristic features of the face are considered pathognomonic of specific medical conditions such as mitral face (mitral stenosis), Hippocratic face (sepsis), lunaris face (Cushing's syndrome, obesity) and other well-known semeiotic *facies*.

From this brief summary, it is evident that building a comprehensive model of face semeiotics able to capture all the available pieces of information is an extremely complex task. Therefore, focusing on a specific application helps to make the problem tractable. Moreover, working with a "real world" setting is expected offer a significantly general framework for further utilization.

That led us to focus on cardiovascular diseases (CVD) and cardio-metabolic risk for which the need of personalized prevention strategies has gained a universal acceptance.

3 CARDIOMETABOLIC RISK

Atherosclerotic cardiovascular diseases (CVDs), including heart disease and stroke, are the leading causes of mortality worldwide (World Health Organization, 2008). The atherosclerotic illness develops insidiously, and clinical manifestations often become evident in its advanced stages. Altogether, frequently, the major events, such as serious health complications, disability and death occur between 40 and 60 years of age. Moreover, the majority of patients who survive a myocardial infarction do not fully recover the ventricular function, and many stroke survivors have physical limitation in the daily activities. This explains why CVDs represent one of the major challenges to the health systems and considerable efforts are profuse to treat clinical manifestations of CVDs. These efforts have granted significant advances with actual improvements in patients' outcome, *quod ad vitam and valitudinem* (Ford et al., 2007).

Despite the success of the pharmacological, interventional, and surgical treatment of the CVDs, it is obvious that all these therapies cannot modify the epidemiological impact of the disease. Moreover, the cost of health systems grows exponentially with the widespread use of complex, and often inappropriate, diagnostic procedures, as well as with population aging. At present, the strategy of prevention, which attempts to modify some pathophysiological factors related to the genesis of the disease, seems to be the only way to limit the epidemic growth of CVDs (Graham et al., 2007). In a recent paper (Pandya et al., 2013) on forecasting cardiovascular disease in the USA through the year 2030, an inversion of the epidemiologic trend was found, which predicts an increase in the overall incidence of cardiovascular disease. This trend is related to two independent factors: the aging of the population and the incidence of obesity and diabetes.

Cardio-metabolic risk is a cluster of risk factors indicative of a patient's overall risk for CVD and type-2 diabetes. These risk factors include: incorrect dietary habits, physical inactivity, smoke, alcohol abuse, abnormal lipid metabolism, hyper-glycaemia, and arterial hypertension (Grundy et al., 2005, National Cholesterol Education Program, 2002, Kahn, 2005). In particular, the metabolic syndrome is characterized by groups of clinical and metabolic features that include high triglycerides, low HDL cholesterol, high blood pressure, high fasting glucose, visceral adiposity (Alberti et al., 2006, Lorenzo et al., 2007). Epidemiological studies have shown that persons with metabolic syndrome have morbidity and mortality for cardiovascular disease 3-4 times increased as compared to control population (Isomaa et al., 2011).

The importance of primary prevention for the decrease of cardiovascular epidemic is well documented by epidemiological studies (Tunstall-Pedoe, 2003) Moreover the impact on mortality of prevention is judged higher in comparison with the effects of evidence-based therapies such as medical and interventional treatments (Ford, 2007; Di Chiara et al., 2009). According to this observation some clinical trials and observational studies have shown a rapid decline in the risk for cardiovascular disease mortality after individual or population-wide changes in diet and/or smoking and in general following a healthy life-style (Capewell et al., 2011). In addition, the favourable impact of prevention on human wellbeing and economics has been estimated by committees of several countries (Capewell et al., 2011, National Institute for Health and Clinical Excellence 2010). Unfortunately, the adherence to the recommended lifestyles and the proportions at goal for blood pressure, lipids, and blood glucose in patients at high risk resulted less than 50% in European surveys (Kotseva et al., 2009; 2010).

Educational programs and lifestyle interventions represent effective tools for reducing cardio-metabolic risk profile and incidence of CVDs (Laaksonen, 2002, Tuomilehto et al., 2001, Vale et al., 2005). However, maintaining a healthy lifestyle frequently needs the counselling and supervision of various health professionals such as dieticians, physical trainers, psychologists and behaviourists. Such a prevention strategy is individually tuned and requires an expensive organization of the health systems.

This evidence suggests the need for new strategies aiming to directly involve people and families in this important task (Aktas, 2004). Self-monitoring is an effective tool to stimulate individual awareness of physical cues and/or behaviours and to identify the barriers to changing behaviour. It may allow the recognition of goals and may provide direct feedbacks guarantying discretion and confidentiality. At the same time, people may choose to activate external communication with prompts such as personal digital assistant or health care professionals (Appel et al., 2003, Wing, 1999). Ward et al., (2010) analysed clinical trials that used self-monitoring in the area of cardiovascular risk management. They indicated 4 major interventions obtainable with self-monitoring strategies: a) education b) self-measurement c) adjustment of (or adherence to) behaviour d) contact with health professionals (Figure 1).

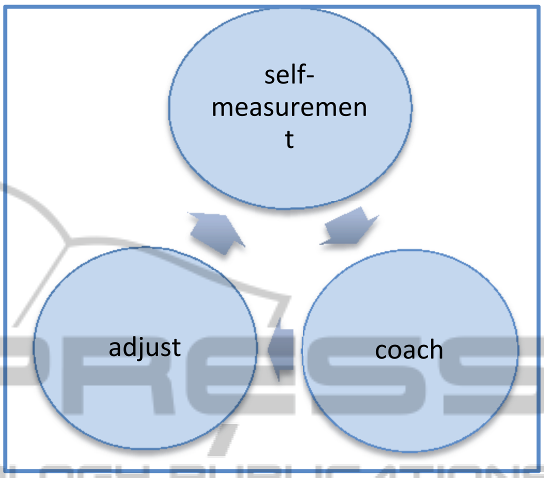

Figure 1: Basic self-monitoring strategy.

As a matter of fact, a rationale alternative to the intensive use of conventional individual coaching is the exploitation of properly developed systems for self-learning and self-monitoring. These systems are expected to help people to change and maintain their lifestyle providing tailored suggestions about nutrition, weight, physical activity, fatigue, and stress according to daily surveys. Moreover, data collected by such coaching systems could be analysed and interpreted by health care professionals so as to support decision-making targeted to the specific individual conditions. This approach has the potential to result highly cost-effective and might foster the diffusion of self-coaching systems with favourable impact on social, physiological, and environmental factors that, at present, remain barriers for the success of large-scale preventive intervention on CVD and diabetes.

4 CARDIO-METABOLIC RISK AND FACE SIGNS

In Table 1 we list a set good indicators of patient's overall risk for CVD and type-2 diabetes. These risk factors are classified in two groups: modifiable and non-modifiable. The majority of them belong to the modifiable category.

In SEMEOTICONS, we propose the adoption of a *digital semeiotics of the face*, that is the computational evaluation of facial signs, focused on those signs that relate to some widely recognized risk factors of CVDs. Consequently, a semeiotic model of the face can be defined taking into account signs concerning: *obesity*, *diabetes*, *hyper-cholesterolemia*, *endothelial dysfunction*, *and psychological status*.

Other general semeiotic signs can be considered to gain more general information about the overall individual's condition.

Each of the above-mentioned risk factors has several observable manifestations on an individual's face.

Table 1: Main cardio-metabolic risk factors.

Modifiable factors		Non-modifiable factors
Overweight/Obesity High LDL cholesterol Low HDL cholesterol High triglycerides hyper-coagulation High blood glucose Hypertension Inflammation	Smoking Unhealthy eating Health disparities Physical inactivity Psychosocial issues	Age Race/Ethnicity Gender Family history

Obesity: The general appearance and several features of the face are relevant indicators of overweight and obesity. The reconstruction of face shape from images and videos and its characterization through a detailed morphometric analysis can, then, serve to localize and evaluate a fatty physiognomy.

Diabetes: The metabolic alterations due to diabetes favour the glycation of proteins and the accumulation of Advanced Glycation End-products (AGE) in the skin (Singh et al., 2001). According to recent results in AGE detection and measurements, autofluorescence stimulated by UV light is a viable solution to detect AGE in sub-cutaneous layer. Diagnostic instrument working in contact with forearm skin are commercially available for clinical use (Meerwaldt et al., 2004). Contact-less measurement of AGEs looks a challenging task. Using hyperspectral-imaging methods is expected to provide a meaningful solution to the problem.

Hyper-cholesterolemia: High level of blood cholesterol could result in some typical signs that have been often related to hypercholesterolemia. In particular, this may be the case of xanthelasmas in the periocular region, as well as the arcus cornealis in the iris border. Both these signs are detectable and reasonably quantifiable in the images of the face with proper morphological/structural analysis methods. Furthermore, one expects that visible - near infrared (VIS-NIR) spectroscopy and imaging may be used to assess the accumulation of cholesterol in the skin of the face and in the iris (Ikawa et al., 2009). As in the case of AGEs, contact measurement of skin cholesterol is described in literature using different approaches (Zawydiwski et al., 2001; Mancini et al., 2002), while contactless measurements are still open to scientific investigation. It must be also pointed out that a deepened knowledge about skin cholesterol accumulation processes and their relation to cardio-metabolic risk would be an important achievement.

Endothelial Dysfunction: Endothelial dysfunction is a major physio-pathological mechanism that leads towards coronary artery disease. Broadly speaking, the endothelium function can be seen as the capability of the endothelium to balance between vasodilating and vasoconstricting substances produced by (or acting on) the endothelium. Endothelial dysfunction can result from and/or contribute to several disease processes (e.g. hypertension, hypercholesterolemia, and diabetes) and it can also result from environmental factors (e.g. smoking tobacco, exposure to air pollution). Endothelial dysfunction is therefore highly informative about individuals' health status. Non-invasive assessment of endothelial dysfunction may be obtained by per cent Flow Mediated Dilation (FMD) measured by brachial artery ultrasound imaging (Peretz et al., 2007). Another simple non-invasive evaluation of endothelium function adopted in clinical practice is based on peripheral artery tonometry (PAT) (Kuvin et al., 2007), which works by measuring Reactive Hyperaemia Index and has been tested in several clinical trials at multiple centres (including major cohort studies such as the Framingham Heart Study, the Heart SCORE study, and the Gutenberg Health Study). A simple alternative to these methods is based on studying microcirculatory blood flow after local heating (Joyner et al., 2001). The key point in the latter approach is that variations in blood supply to sub-cutaneous districts result in variations of skin optical properties ("colour"). Consequently, an accurate analysis of temporal sequences of face images in the visible and a near-infrared band is a practicable way to evaluate elementary hemodynamic parameters. These can relate to heart rate, oxygen saturation,

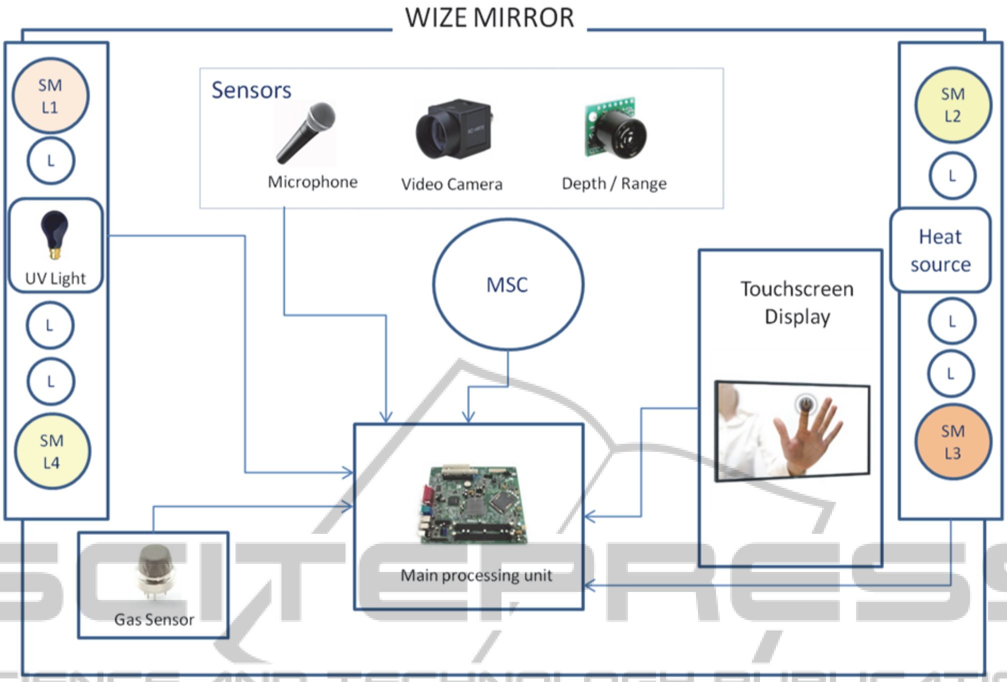

Figure 2: Wize Mirror hardware scheme, including Multi Spectral Camera (MSC), standard lights (L) and multicolour lights (SMLi, i=1, ...,4).

peripheral resistances and also endothelial function. Actually, after providing a controlled thermal stimulus to trigger a vasodilatation, the evaluation of such hemodynamic response gives a measure that can be correlated to the endothelial function. Moreover, the analysis of heart rate variability can serve to the characterization of the autonomous nervous system.

Psychological Status: The morphological appearance of human face can reveal useful information about an individual's mood, anxiety, and status of fatigue (Pantic and Bartlett, 2007). Facial expression recognition and facial biometrics in 3D space are expected to serve this scope. Integration of these descriptors with other well-established cardio metabolic risk signs into self-monitoring systems is worth of investigation. Correlation of facial descriptors of psychological status with questionnaires can help to better understand their role to assess an individual's wellness status.

Other Semeiotics: Among the other signs that can be related to well being status and may potentially relate to different individual conditions going from fatigue/tiredness and stress to specific diseases, the following are worth of consideration:

– Face colorimetric features, e.g. pallor, jaundice, redness.
– Regional skin surface temperature in the face.
– Respiratory rate.

5 SEMEOTICONS APPROACH

A main technological objective in SEMEOTICONS is the development and design of a multisensory system hosted into a hardware platform having the exterior aspect of a conventional mirror (*Wize Mirror*). A conceptual drawing of the Wize mirror is shown in Figure 2.

It will include cameras and depth sensors to enable 3D reconstruction of the user face. This will be used for morphological analysis (overweight and obesity description, feature recognition for psychological status evaluation) as well as to drive other acquisitions phases (normalization of face position and orientation). Properly designed multispectral cameras will allow obtaining data on the cardio-respiratory system (heart rate, blood-oxygen saturation, endothelial function, respiratory rate), on the presence of products of glucose and lipid metabolism in the skin. The inclusion of other sensors is also planned. In particular, the *Wize Sniffer*, i.e. a gas sensor able to analyse exhaled gases, will help to monitor lifestyle habits (smoking and alcohol consumption). The Wize mirror will include a lighting system for image acquisition, UV light to stimulate fluorescence mechanisms and

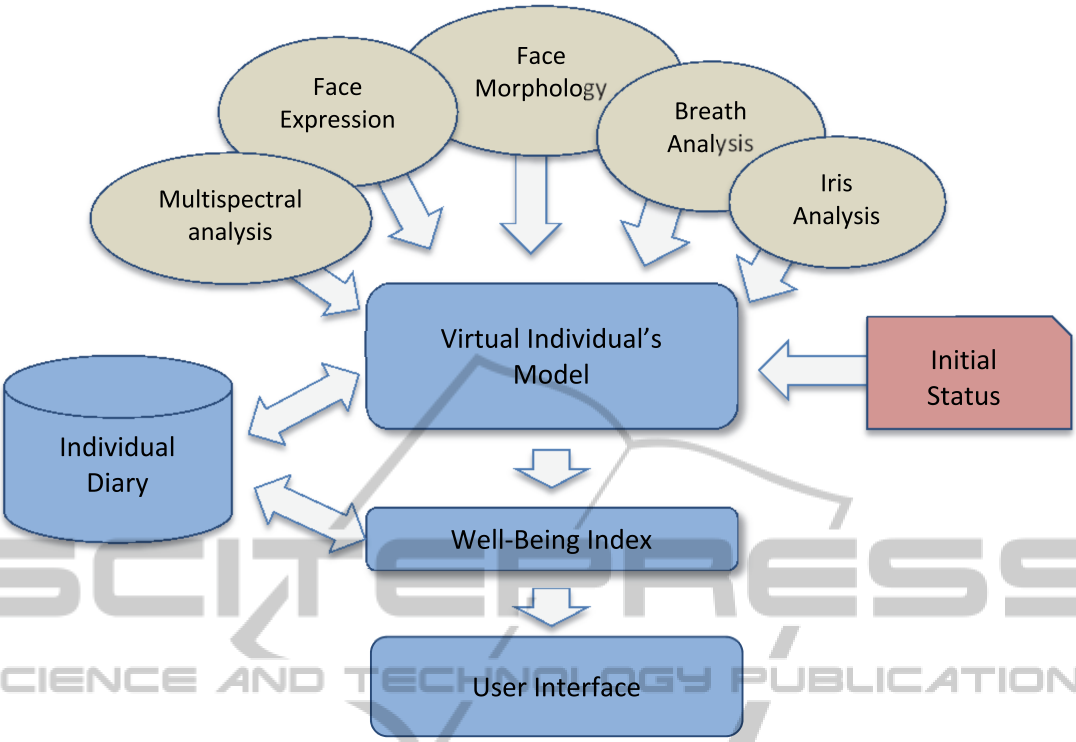

Figure 3: Wize Mirror Virtual Individual Model.

thermal lamps for heat testing of endothelial function. User interaction will occur by an integrated touch screen.

According to section 4, images and signals have to be mapped into a set of descriptors, each of them being related to some aspects of cardio-metabolic risk. Afterwards, to obtain indication about the individual's health status and discover noxious lifestyles, the computed descriptors, which are intrinsically disaggregated entities, need to be integrated into a high-level representation able to capture the individual as a whole. For that aim, one has to take into account individual's peculiarities, including both family and personal history. The Virtual Individual Model (VIM) implemented in the mirror will carry out the integration task. The major requirement on VIM is the ability to detect and signal significant changes of face semeiotics to assist user behavioural change. Therefore, an absolute assessment of individual wellness is not mandatory.

The model instantiation process shall include a preliminary user-profiling phase to be accomplished at the beginning of any self-monitoring activity. This phase aims at defining the psychophysical characteristics of the individual at baseline. These should be derived on the ground of previous medical examinations, personal history, and interactive psychological questionnaires.

Therefore, the user profile will serve to define the initial status of the VIM and may also provide important constraints on the user-interface preferences. According to this approach, the temporal evolution of the model will describe the changes of the user's psychophysical status starting form a known initial condition. In general, past VIM history would enter the computation of the current status and is expected to contain useful indications for user advising and coaching. For these reasons, a track of the VIM evolution will be retained in the Individual Diary.

The internal VIM representations and the related adaption rules are designed to operate at the level of input data and would be, in general, unsuitable for user communication and interaction. For this aim the system would compute the WBI, which represents a synthetic description of VIM state. The WBI will be a multidimensional entity whose components should measure the different aspects of individual lifestyle appropriateness (e.g. food, physical activity, psychological status, noxious habits). According to the profiling phase, WBI components would be properly presented to the user along with educational and coaching messages.

To summarize, detection and integration of signs derived from the semeiotics of the face should lead to build sensitive equipment to self-monitor the psychophysical state and, possibly, elaborate suggestions useful for optimizing the personal life style and to trap the major cardio-metabolic risk factors.

In this perspective, SEMEOTICONS aims at building an innovative virtual individual's model, which is based on a set of objective signs, closely related to cardio-metabolic risk profile and derived from external physical examination of the face. The model should serve to evaluate a subject well-being status over time and allow early detection of improper lifestyles as well as potentially dangerous conditions mainly related to cardio- metabolic risk.

6 CONCLUSIONS

Medical semeiotics, in the era of magnetic resonance, computed tomography and molecular biology, is still a valuable resource that may be useful in every condition and location independently of other structural facilities. The development of advanced imaging and biological diagnostic techniques has probably attenuated the interest for developing technological tools based on data obtained from *simple* semeiotics. Nevertheless, the role recently acquired by self-monitoring and self-training has opened new, significant perspectives to this well-established branch of classical Medicine.

Semeiotics offers a sound methodological frame to build new computational tools also exploiting innovative multi-sensing devices. The adoption of a *digital-semeiotics approach* is expected to ease the implementation of virtual individual models able to effectively assist people in keeping a healthy life-style.

In this view, SEMEOTICONS *Wize Mirro*r will be a new kind of self-monitoring system. Its architecture will be absolutely non-obtrusive and will be able to use personal data for coaching and learner-adaptive messaging.

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