SMART MEDICAL SYSTEMS WITH APPLICATION TO NUTRITION AND FITNESS IN SPACE

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ABSTRACT

Smart medical systems are being developed to allow medical treatments to address alterations in chemical and physiological status in real time. In a smart medical system sensor arrays assess subject status, which are interpreted by computer processors which analyze multiple inputs and recommend treatment interventions. The response of the subject to the treatment is again assessed by the sensor arrays, closing the loop. An early form of "smart medicine" has been practiced in space to assess nutrition. Nutrient levels are assessed with food frequency questionnaires, which are interpreted by flight surgeons to recommend in-flight alterations in diet. In the future, sensor arrays will directly probe body chemistry. Near infrared spectroscopy can be used to noninvasively measure several blood and tissue parameters which are important in the assessment of nutrition and fitness. In particular, this technology can be used to measure blood hematocrit and interstitial fluid pH. The noninvasive measurement of interstitial pH is discussed as a surrogate for blood lactate measurement for the development and real-time assessment of exercise protocols in space. Earth-based application of these sensors are also described.

Smart Medical Systems – A Definition

Medicine has always been practiced through a close and personal relationship between patient and physician. While nothing can replace this important emotional bond, there are certain circumstances where direct contact between the patient and his or her doctor can, at times, be difficult to accomplish. An example of this is space travel and exploration. In the current space station program, astronauts have limited confidential time to discuss health issues with the flight surgeons on the ground. This situation will become even more difficult during a multi-year mission to Mars, where there will be periods of time where astronauts are out of communication with support personnel on the ground, and even nominal communication from Mars will be delayed 22 minutes in each direction. In addition to receiving advice from personal physicians, patients in extreme environments sometimes need to be treated for medical emergencies. Recently a scientist at the South Pole had to be evacuated under extremely harsh conditions in order to receive treatment for breast cancer. Evacuation of personnel during interplanetary exploration may be impossible. Evacuation from the International Space Station, in low earth orbit, would be difficult, costly, and time consuming, and further may not be feasible in emergency situations. Smart medical systems will provide tools for space travelers and others in remote environments to receive medical advice and treatment at times when they cannot have personal contact with their physician.

Smart medical systems are composed of multiple feedback control systems, each containing 3 basic components (Figure 1) (a) sensing elements to assess physiological or medical status, (b) processing units to analyze sensor inputs to determine if health status is normal, or whether treatment is required, and (c) treatment effectors, possibly accompanied by an embedded intelligent system, that supervises the application of treatment. Within each control system, multiple sensors assess the status of a subject and feed information to a computer processor for analysis. Treatment recommendations are made and implemented, thereby impacting patient outcome. Results of an intervention are assessed by the sensors, and hence close the loop. Each feedback control system has the capability to act as a smart medical system itself, wherein pattern recognition of sensor data and medical decision making allow for effectors to deliver treatment with minimal human intervention. However, parallel and cooperative activity among many such systems creates a system of systems, which will function as a larger smart medical system. In this case, analysis of real time data involves input from multiple system sensor arrays, which may be using different technologies to assess physiological measures. Treatment decisions and the delivery of interventions occur in a coordinated way across systems to maximally benefit patient outcome.

As an illustration of a basic smart medical system, we will consider control of glucose in a diabetic patient. In these patients the inherent, biological feedback mechanism that regulates plasma glucose concentration by controlling insulin secretion rates is defective because the treatment effector (the pancreas) is inoperable. A smart medical system could potentially overcome this defect and improve the quality of life for these patients. Currently diabetic patients must test themselves 4-5 times per day, and manually adjust their insulin dose in response to the sensed glucose level. This is a primitive form of a smart medical system. The patients draws their own blood, which is measured by the glucose meter (one of the sensors in Figure 1). The processor, in this case, is the patient, who is trained, by the physician, to adjust their insulin dosage or food intake (the treatment) in response to the sensed level of glucose. The effect of the treatment is assessed by the next sensor measurement, several hours later. While the landmark Diabetes Control and Compliance Trial illustrated significant reduction in long term complications with frequent measurement of blood glucose[1], fingersticks several times per day are difficult for many patients. This smart medical system is evolving with the development of innovative sensing and therapeutic technology. There are now implantable sensors that can continually monitor glucose levels and report them to a computer every 5 minutes[2], requiring no intervention from the patient. Furthermore, these sensors can be coupled with implantable insulin pumps. Currently, the pumps are programmed to provide a constant basal level of insulin. Continuous monitoring provides information to the patient, who is still the "data processor", to adjust their insulin in response to daily changes in activity[3]. The next evolution in this smart medical system will be the coupling of the glucose sensor to the insulin pump, through a smart computer processor, to provide minute-to-minute, unassisted control of blood glucose levels.

Smart Medical Systems To Assess Nutrition During Spaceflight

Inadequate food intake has been observed on most space missions[4-6]. The obvious consequence of this is inadequate intake of both macro- and micronutrients. The reasons for decreased consumption are unknown, however one possible explanation is that food may taste different in space because of either nasal congestion from bodily fluid shifts or the effects of recirculated air on odor perception. Another possible explanation is that the lack of textural variety in early space food have may have discouraged adequate consumption[4]. On shorter flights space motion sickness may have decreased astronaut appetite[7].

Only during the Skylab missions was macronutrient consumption at recommended levels. Astronauts on Skylab had more palatable food, since both fresh and frozen foods were available to this crew[4]. These crews were participating in metabolic experiments, which required daily discussions with ground personnel and reports of any uneaten food. To maintain experimental requirements for intake of specific nutrients (e.g., calcium, protein), the nutritional value of uneaten foods were quickly calculated, and the crew was advised on supplements that were required to maintain intake of these key nutrients. This system therefore ensured adequate dietary intake, and represents the effectiveness of reporting consumption to the ground crew to ensure adequate dietary intake.

Daily reports from the crew of exact dietary intake are not feasible on the International Space Station (due to the amount of time required), and would be even harder on planetary mission. Nonetheless, this early work provided the model for the development of a smart medical system – a means to quickly, and easily assess dietary intake during long-duration space station missions.

The Nutritional Biochemistry Laboratory at the Johnson Space Flight Center developed a food-frequency questionnaire (FFQ) that is used by astronauts during space flight to assess dietary intake. This was developed toward the end of the NASA/Mir program in the late 1990's, and is currently in use on the International Space Station[6]. The FFQ is a computerized program and is scheduled for completion weekly by the ISS crewmembers (Figure 2). Foods are grouped in categories (e.g., beverages, meats, vegetables), and food items with similar nutrient content are combined for a single response. The crewmembers enter the number of food packages consumed over the past week. The data are stored in a file, which is down-linked to the ground soon after completion. The data are then processed through a computer database to provide estimates of the intake of six key nutrients (water, calories, protein, iron, calcium, and sodium), and reports are prepared and submitted to the flight surgeon on the ground. The intent of the FFQ is that during the mission flight surgeons will review the questionnaires and make near real-time recommendations on how astronauts could improve dietary intake[5]. In addition, astronauts monitor their body mass on a regular basis, and this data is interpreted along with the dietary intake data – to provide a more complete understanding of nutritional status. In this example of a smart medical system, the FFQ and the body mass analyzer are the data collection elements, or sensors, in the smart medical system. The FFQ data are processed by a computer into the key components (nutritional elements), which were then used by the flight surgeon to make "treatment" or dietary corrections. The success of treatment may be evaluated with the successive questionnaires and body mass measurements.

One could envision that this system might evolve to remove the flight surgeon from the loop. An intelligent computer program could evaluate the FFQ, and make recommendations to the astronaut, based on available food stores in the spacecraft. However, the psychological aspects of taking advice from a machine, compared to a remotely located physician, would certainly have to be studied. Other nutritional issues in space may also lend themselves to the development of smart medical systems. These include bone and muscle loss, renal stone risk assessment, iron and hematological changes, and the need to adjust dietary intake for the energy costs of exercise in space[4,8].

New Technology for Smart Medical Systems

Smart medical systems for nutrition would ideally involve little input from the astronauts themselves, since the astronauts are very busy with other tasks. In this regard, sensors which could evaluate the effect of nutrition on the astronaut's body might be the next step in the evolution of smart medical systems for nutrition. These sensors should be able to evaluate blood and urine chemistry frequently and in real-time. Currently, NASA flies a commercially available clinical blood analyzer that is capable of accurately measuring blood pH and ionized calcium using capillary blood taken from a finger stick. The system has the potential to also measure glucose, sodium and potassium, though superior results were obtained from a venous, rather than capillary blood samples[9].

The ideal sensor systems would not require a blood draw and would be able to make measurements on a frequent basis, such as during exercise or severe exertion (e.g. during a extravehicular activity). Near infrared spectroscopy (NIRS) provides the technology for such noninvasive measurement. Near infrared light passes through skin and bone and analysis of the light that passes through a finger or is reflected back from a muscle can be used to assess blood and tissue chemistry. Arterial oxygen saturation and heart rate are routinely measured noninvasively using NIRS (pulse oximetry). Recent research into medical applications of NIRS has extended the range of blood and tissue parameters that can be measured. Many of these are relevant to smart medical systems for nutrition assessment in space.

Spaceflight anemia has been observed on almost all space missions. Red blood cell mass is decreased approximately 10-15% below preflight levels, and this is attained after approximately 2 weeks of flight[4,10]. Early results from NIRS-based systems that noninvasively measured total hemoglobin concentration and hematocrit levels for human subjects have recently been reported. Jeon et al showed that hemoglobin could be measured using 5 light emitting diodes in the wavelength region between 569 – 975 nm. The authors reported an estimated accuracy of approximately 1 g/dL in their initial study[11]. Noninvasive hematocrit measurement has been demonstrated on surgical patients with large variations in blood hematocrit. These measurements were made with a full spectrum fiber optic sensor in the wavelength region between 581 and 1000 nm[12]. The sensor used in this study is shown in Figure 3. Measurements were made simply by placing the sensor on the surface of the skin. Within single subjects, the measurement accuracy was excellent, 1 Hct %, however measurements between subjects were degraded due to variation in subject skin color, fat content, and instrument variability. Current research is focusing on developing methods to eliminate these factors and improve measurement accuracy for all NIRS-based chemical measurements. These noninvasive measurement techniques may have application in assessing hematology during spaceflight, and help to ensure astronaut health and safety.

The advantage of these spectroscopic-based measurements is that they do not require any blood to be withdrawn from the subject. This facilitates multiple measurements over time, and even continuous measurements, as the sensor can be attached directly to the subject. Another advantage of the spectroscopic approach is that it provides a platform for sensing multiple species. Once the spectra are acquired from the subject, they can be processed through different calibration equations that calculate several different blood or tissue analytes from the same spectral information. It has been recently demonstrated, in an in-vitro study, that it is feasible to simultaneously measure the concentration of sodium, potassium and calcium ions in whole blood from spectra collected in the range of 500 – 2200 nm[13]. A device to measure these ions transdermally in blood, or automatically in urine through a spectroscopic cell in the waste evacuation line might be important in a smart medical system for spaceflight. Loss of plasma volume and bone degradation during space flight result in an increase in serum and urinary calcium levels, increasing the risk for renal stone formation[4]. Blood levels of sodium and potassium have also been noted to change during spaceflight. This bears watching since sodium intake may be increased through food preservatives used in packaged space food and excessive sodium exacerbates calcium loss[14]. Noninvasive sensors that can monitor either urinary or blood levels of these important electrolytes could be used to guide application of nutritional therapies (countermeasures) to address bone loss and other nutritional imbalances.

Another parameter that can be measured noninvasively using NIRS is tissue pH. Tissue pH, or in this case, pH of the interstitial fluid, is an indicator of anaerobic metabolism. Tissue pH has been measured transdermally with NIRS in muscle tissue during vessel ischemia in rabbits[15], hemorrhagic shock in swine[16], and recently in patients with mild hypotension induced by heart surgery under cardiopulmonary bypass[17]. The noninvasive measurement of interstitial fluid pH may have application in the development and assessment of exercise as a countermeasure to improve muscle strength under microgravity conditions. Carefully controlled exercise regimens will also require interventions in nutrition to match energy requirements.

Skeletal Muscle and Cardiovascular Alterations with Space Travel

Space travel has detrimental effects on skeletal muscle structure, metabolism and function. The lack of gravity in the space environment reduces the load on the muscles that support body weight and motion, leading to reductions in muscle size, strength and endurance, as well as to breakdown of muscle protein and changes in muscle fiber type distribution[18]. It has been reported that a brief (2-5 days) exposure to weightlessness can result in a 15% loss of strength in the postural muscles[19]. Experimental studies have been conducted to investigate the genetic, cellular, and functional effects of weightlessness on skeletal muscle in humans and rodents. These studies have shown that just 5 or 6 days in microgravity can cause significant atrophy in skeletal muscle, reducing motor capacity, strength, and endurance properties[18-20].

In addition, space travel impairs the cardiovascular system's ability to readapt to partial or full Earth's gravity (1G). Following short (15 days) and long-duration (> 3 months) missions, astronauts experience reduced exercise capacity upon reentry[19,21]. Measurements of cardiopulmonary responses to exercise after space flight have consistently documented reductions in exercise capacity[21]. The combined effects of the functional reductions in the skeletal muscle and the cardiovascular system's capacity have detrimental effects on the astronauts' physical performance. In the case of an emergency, the lowered physical performance induced by space travel deconditioning could be task, mission, or life threatening.

Exercise as a Countermeasure for Cardiovascular and Muscle Deconditioning

The detrimental effects of weightlessness exposure can be counteracted to some extent with exercise training. However, the optimal amount (intensity, duration, and frequency) and type of exercise needed to counteract the detrimental effects of microgravity on the astronauts' work capacity is not known. The current Countermeasures System (CMS) in the International Space Station (ISS) includes a treadmill, a cycle ergometer, an interim resistive exercise device, and a hand grip dynamometer. Astronauts perform various exercise routines on these devices on a daily basis while their responses are assessed by means of a heart rate monitor, a blood pressure/ECG monitor, and/or the medical equipment computer. The goal of exercising on these countermeasure devices is to maintain the astronauts' physical fitness as close to preflight levels as possible. Recently, as a result of these countermeasures (and potentially others), astronauts have been able to exit the space shuttle unassisted, upon reentry to earth. However, the lengthy amount of time (~ 2 hours/day) dedicated by the astronauts to maintaining fitness while at the ISS precludes them from performing other desirable scientific endeavors. Ideally, knowing the time course of certain physiological variables used as markers of fitness and the precise effect of various exercise training regimes on these markers would facilitate optimization of training programs to avoid dedicating excessive time to training.

Monitoring the Effects of Exercise Training Programs

A practical and simple way of monitoring changes in fitness level is to track the slope of the linear relationship between heart rate and work rate at various exercise intensities (typically three) that do not result in blood lactate concentrations above resting levels[22]. Consequently, the astronaut is required to perform an incremental exercise protocol with step increments of ~50 watts and 5 min duration. Heart rate is typically measured using commercially available heart rate monitors which consist of a chest strap with electrodes and a coded transmitter and a wrist receiver. The average heart rate at the end (~15 sec) of each incremental step is recorded and plotted versus work rate. The slope of the heart rate–work rate relationship is then calculated and compared to pre-flight values to evaluate the effect of the astronaut's exercise training program in counteracting space travel deconditioning. The number of opportunities for intervening and adjusting the exercise training regime depends on how frequent this evaluation is made. Even though this method is very simple and effective, the heart rate response is highly susceptible to variations due to multiple factors, such as, temperature, weightlessness, stress, time of the day, humidity, previous meal or physical activity, etc.[22].

Traditionally, maximum oxygen uptake, (VO_2max), the highest rate of oxygen uptake achieved during an incremental exercise test, is considered the best index of cardiovascular functional capacity. However, VO_2max depends on cardiovascular factors, such as stroke volume and cardiac output, and can be sustained only for short periods of time (< 1min). An alternate index of fitness and predictor of endurance performance is the blood lactate response to exercise[23-25]. This response is dependent on peripheral factors such as the muscle fiber type or the number of mitochondria, as well as cardiovascular factors. Exercise at intensities engendering steady blood lactate concentrations can be sustained for long periods of time (>30 min)[24,25]. Since endurance exercise is typically performed at the highest sustainable intensity, the blood lactate response seems to be a better predictor of endurance performance than VO_2max[23].

Several studies have showed that the blood lactate responses to maximal incremental or submaximal constant work rate exercise have characteristic time profiles which can be used as indicators of endurance performance[23-26]. In many cases, parameters estimated from the lactate concentration dynamic response to ramp- or step-changes in work rate have showed better correlation and greater sensitivity to improvements in exercise performance than VO_2max. In particular, almost all investigations have shown that the work rate and VO_2 associated with various blood lactate parameters (e.g., lactate threshold, maximal lactate steady state) improve to a much greater extent with training than VO_2max [23-26]. Furthermore, it has been suggested that training to improve the blood lactate response to exercise is the type of training required to improve endurance performance[23].

The blood lactate response has also been used as a tool for exercise prescription[23]. It has also been suggested that training intensity be based on one or more parameters derived from the blood lactate response to exercise. Unfortunately, since estimation of desired lactate parameters from this response requires multiple blood samples, various noninvasive methods of identifying blood lactate parameters from alternate responses to exercise (e.g., heart rate or oxygen uptake) have been developed and evaluated[22,27-29]. However, the most accurate application of blood lactate concentration in developing exercise training programs comes still from direct measurements of blood lactate. Current availability of rapid-response, low-cost, portable blood lactate analyzers requiring minute amounts of blood has made the use of lactate parameters more accessible to field testing and to a larger athletic population. In spite of these advances leading to a widespread use of blood lactate parameters for predicting performance, evaluating training, and designing exercise programs on Earth, an alternate method not requiring multiple blood samples that provides similar information would be desirable for space travel applications.

One of the reasons for the success of the blood lactate method in predicting, designing, and evaluating exercise outcomes is that it reflects to a great extent the pattern of the muscle lactate response to exercise. Since the latter requires the use of serial muscle biopsies to provide enough data to characterize the tissue lactate response to ramp- or step- changes in work rate, it is understandable why it is not commonly used, in spite of providing the most reliable method to assess muscle lactate parameters. It would be ideal to develop a smart medical system that could measure the lactate concentration in the exercising muscles noninvasively and continuously. The muscle lactate response to exercise could then be processed to estimate desired lactate parameters, used to adjust training intensity or to simply monitor the response during an exercise session. To our knowledge, there are no such devices available or in development at the present time.

Hydrogen ions are produced, stoichiometrically, when there is net lactate production by the cell. During exercise, accumulation of lactate reduces cellular pH and subsequently interstitial and venous pH. In skeletal muscle, hydrogen ions (H^+) are some of the by-products of cell metabolism when ATP is hydrolyzed to provide energy for muscle contraction. In addition, hydrogen ions are consumed during phosphocreatine breakdown and oxidative phosphorylation. Therefore, when the total rate of ATP formation is mainly provided by these two energy systems and matches the rate of ATP hydrolysis, no net accumulation of H^+ occurs. On the other hand, anaerobic glycolysis (i.e., resulting in lactate formation) does not consume H^+ and under conditions of ATP homeostasis, will result in H^+ accumulation.

The availability of noninvasive techniques that can measure intracellular pH in working muscle continuously, such as magnetic resonance spectroscopy (MRS), has provided dynamic information on tissue pH changes. Indeed, Zanconato et al[30] have measured the time profile of intracellular pH in calf muscle of adults performing incremental plantar flexion exercise using ^{31}P-MRS and showed a slow (7.07 to 7.05 at moderate intensities) and a fast phase (7.05 to 6.75 at high intensities) of pH decrease in 75% of the subjects. This biphasic behavior is similar to the one observed in arterial pH during incremental exercise on a cycle ergometer and mirrors the changes in muscle lactate concentration[31].

In summary, under resting conditions or during exercise of moderate intensity most of the ATP synthesized to sustain muscle activity is derived aerobically. The glycolytic contribution to ATP formation during moderate exercise is minimal (<2%). When the glycolytic contribution to muscle ATP formation increases, such as during high intensity exercise that engenders blood lactate values between 1 mM and 4 mM, the $[H^+]$ in the exercising muscles also increases.

Smart Medical Systems Involving Noninvasive Interstitial pH Sensors

Continuous monitoring of tissue pH in working muscles requires serial biopsy samples every 10 sec or the use of MRS on a large muscle mass[32,33]. However, in space, both methods are impractical and thus cannot be used on a routine basis. Nevertheless, during high intensity exercise, the pH of the parenchymal cells, the interstitial fluid, and the venous blood surrounding the muscle decreases in proportion to the exercise intensity[34]. In addition, there is a good correlation between muscle pH and lactate concentration during exercise[34,35]. Therefore, the venous blood or interstitial pH response to exercise can be used as a potential marker to monitor fitness level or exercise training programs.

The time profiles of the decrease in arterial blood pH observed during incremental [36,37] or constant work rate[37,38] exercise are highly correlated with the increase in arterial lactate concentrations. However, regulation of arterial pH depends on the magnitudes of the exercise intensity and ventilatory response, changes in arterial PCO_2, and varies from subject to subject. Venous blood pH, on the other hand has the advantage of representing only the muscle capillary bed and consequently is more representative of tissue pH changes than arterial pH. At rest, the femoral venous (7.37- 7.43), arterial (7.40 ± 0.03), and interstitial (7.38 ± 0.02) pH values are very similar, while tissue pH (7.04 – 7.17) is typically a few units lower than interstitial pH, both at rest and during exercise[34]. The amplitudes of the exercise induced decreases in venous blood and interstitial pH are similar during moderate and heavy intensity exercise[34]. However, during very heavy exercise, interstitial pH decreases to a larger extent than femoral venous pH[34]. This may be in part due to the fact that a fraction of femoral venous blood comes from inactive tissues and inactive parts of the quadriceps. Thus, continuous monitoring of interstitial pH during exercise might provide alternate markers of fitness that can be used in the design and evaluation of exercise training programs. The main advantages of monitoring interstitial pH during exercise instead of blood lactate are: (a) the interstitial space is anatomically closer to the working muscles than the blood compartment and (b) interstitial pH can be monitored noninvasively and on a continuous basis.

Therefore, a smart medical system could be developed to measure interstitial pH in the exercising muscles noninvasively and continuously using NIRS technology[15]. The interstitial pH response could then be processed to identify and estimate new sensitive markers of fitness that are based on its characteristic time profile to various exercise stimuli. This information would be valuable in providing guidelines for adjusting training intensity and for simply monitoring the response during an exercise session, either in space or on earth. Once the relationship between interstitial pH and energy expenditure is developed, this information could be used as part of a smart medical system to link nutritional intake to demand.

Earth-Based Applications of Smart Medical Systems Developed for Space

Smart medical systems for assessing interstitial fluid pH would not only have application for assessing and guiding exercise protocols in space, but would also be applicable to the training of athletes on earth. The same sensor system will also have utility both in space and on earth for the assessment and treatment of traumatic injuries. Muscle pH has been shown to be correlated with blood loss during hemorrhage in swine and has the promise of providing an indication of successful resuscitation[39,40]. One can envision the day where a NIRS-based sensor measuring tissue pH, hematocrit and blood sodium concentration might be used to assess the severity of shock and guide the administration of resuscitation fluids so that just enough fluid is given to restore aerobic metabolism, but not too much to cause anemia and increased sodium levels. This sensor might be used in a feedback loop with an automated pump which controls the type and rate of fluid administration, adjusting on a minute-to-minute basis, as determined by the tissue and blood sensors.

Sensors developed to assess hematocrit during spaceflight can also have significant impact on earth. Anemia is a world-wide problem[41]. In many countries over 40% of the women of reproductive age are anemic, increasing the risk of maternal and child mortality. Anemia negatively impacts child development and behavior. Anemia in young adults impairs work capacity and productivity, especially in agricultural communities[42]. There are several causes for anemia, particularly in economic and socially disadvantaged populations. These include 1) nutritional deficiencies, particularly in iron-rich foods, 2) malaria, 3) intestinal parasites, 4) HIV and other infection diseases, and 5) genetic hemoglobinapthies[41]. Screening is an important first step in identifying populations at risk and implementing strategies to correct nutritional deficiencies and other health problems. The only portable technology currently available to measure blood hemoglobin concentration in the field is the HemoCue system; a spectrophotometric system requiring a blood sample. This system has been found to provide good data, however it exposes the health care worker to blood-borne diseases and the disposable cuvettes required for the system are expensive[42], limiting it's use. The NIRS hematocrit sensors being developed to assess spaceflight anemia may provide a noninvasive, lightweight, portable, and hopefully inexpensive method to effectively field screen significant populations for anemia.

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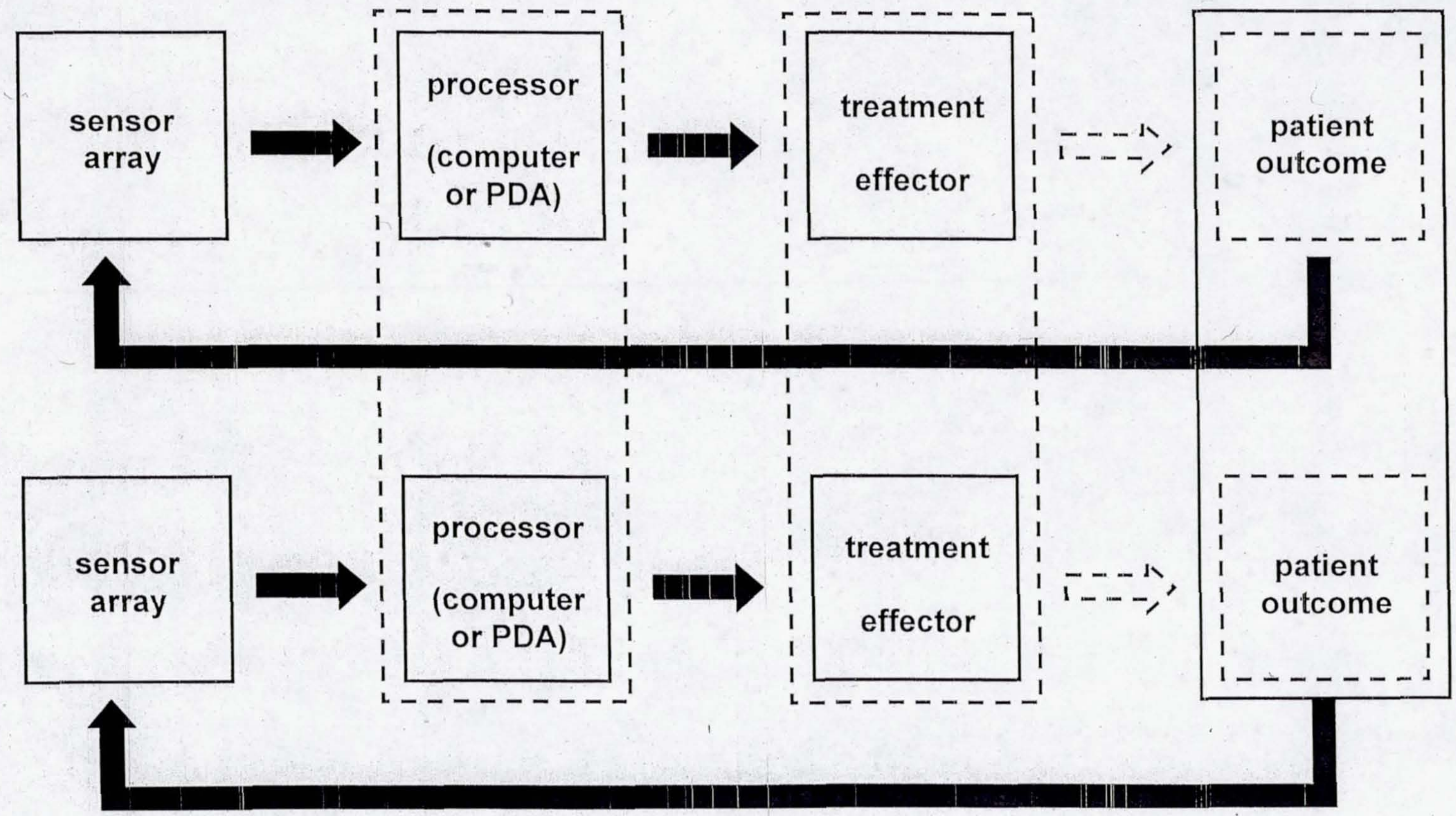
Figure Captions

Figure 1. Schematic diagram of a smart medical system showing two feedback control systems. Within each system multiple sensors assess the status of the subject and feed information to a computer processor for analysis. Treatment recommendations are made and implemented, impacting patient outcome. Result of the intervention is assessed, closing the loop.

Figure 2. Computerized Food Frequency Questionnaire used on the International Space Station. (a) Introductory screen, (b) top portion of the data input screen.

Figure 3. Noninvasive fiber optic sensor for measuring blood hematocrit and tissue pH. (a) Placed on forearm to make continuous measurements (b) Close-up of sensor. Outer ring of optical fibers carries illumination light to tissue. Inner bundle of fibers carries light to a spectrometer for analysis.



sensor array
processor
(computer or PDA)
treatment effector
patient outcome
sensor array
processor
(computer or PDA)
treatment effector
patient outcome