## Good Morning.

Our experiences in both Afghanistan and Iraq have again demonstrated that the success of military missions is highly dependent on the soldier's ability to arrive on the battlefield exquisitely trained, in peak condition, and perhaps more importantly, to maintain peak physical and cognitive performance for the mission duration.

We in DSO are committed to developing new strategies to preserve the peak health and performance of our deployed troops, even in the face of extreme battlefield and environmental conditions.

There are four major thrusts which define DARPA's strategy: \* First, we must develop novel approaches to maintain peak physical and cognitive performance in the face of sleep deprivation, inadequate nutrition, and harsh environmental conditions such as heat stress.

\* Second, we seek to transform the paradigm of battlefield medical care so that it parallels the ongoing transformation in operational concepts and missions.

\* Third, we will develop biotechnology to markedly enhance the warfighter's ability to survive and recover from a severe acute injury, as well as his/her ability to regain normal function following convalescence.

\* Finally, we will pioneer new ways to monitor, predict, and defend soldier health against both inflicted and indigenous diseases, which remain constant threats to mission success.

Solving these threats to soldier health and performance is the most recent addition to DARPA's biorevolution.

The first DARPA foray into maintaining human combat performance is in the area of sleep deprivation.

While it is certainly possible to keep one's eyes open with frequent visits to Starbucks, those of us who have pulled "all-nighters" will certainly remember the irritability, poor judgment and memory errors that result from a lack of normal physiologic sleep.

This degradation in mental performance may be acceptable for college students, but not for those who make critical life or death decisions during battle.

Unfortunately, current approaches are only partially effective in warding off sleep, and they are woefully lacking in their ability to sustain peak cognitive and psychomotor acuity.

As such, the DARPA program is exploring the limits of sleep biology, and we seek new ideas.

Is there a physiologic substitute for periods of normal sleep? What are the biological reasons why some animals can stay awake for extended periods without loss of function?

Are there central nervous system detours around fatigued neural pathways? Early success has come by exploiting approaches already proven to improve memory impairment in patients with Alzheimers dementia.

Specifically, the DARPA program has now demonstrated that the ampakine class of drugs can reverse memory loss and psychomotor degradation after 30 hours of sleep deprivation.

In a related effort, through the use of functional brain imaging, we have indications that some neuronal circuits are more resilient to sleep deprivation than others, thus offering the possibility that cognitive training which reinforces use of resilient brain pathways might markedly improve performance after sleep deprivation.

This program is still in its early stages, and we continue to seek new ideas.

Another area often taken for granted is basic nutrition. While a typical adult requires 1500 - 2000 calories per day, Special Forces fighters may require more than 6 - 8,000 calories a day, though it is practically impossible to consume much more than 5,000 calories a day - equivalent to an MRE and 30 Power Bars.

This relative caloric deprivation leads to catabolism of essential tissues, including skeletal muscle, and inevitably results in profound weight loss and degradation of performance.

Our DARPA program seeks ways to improve the efficiency the body's energy utilization so that fewer calories are required; moreover, we aim to explore the very concept of adequate nutrition. We want food to be much more than just calories.

Therefore, we are asking questions such as whether specific foods or nutrients can be used to bolster immunity, or minimize muscle fatigue, or improve memory.

As part of this thrust, we are also exploiting the critical relationship between body temperature and optimum physical performance. Current data indicate that for trained athletes, the physiologic limit to physical performance, also known as "hitting the wall," is related primarily to the body reaching a critically high core temperature as a result of the metabolic activity of muscle.

When this critical temperature threshold is reached, performance degrades rapidly.

Thus far, we have demonstrated that by using a prototype thermoregulatory device and intermittent cooling, we can instantaneously improve peak performance, as well as dramatically enhance training over time.

We are interested in exploring other novel approaches.

The second major thrust area in which we are seeking new ideas focuses on improving survival on the battlefield.

One program, soldier self-care, has already demonstrated some dramatic results.

This program recognizes that, as small units become more dispersed, medical care becomes less and less available, and medical crises such as extreme pain and severe bleeding will need to be controlled by the soldier, perhaps for extended times, until medical evacuation.

We at DSO are seeking techniques so that soldier, by himself or herself, can maintain physiologic homeostasis in the face of otherwise debilitating injuries.

Successful approaches will not only improve survival from the initial injury, but will also allow soldiers enough residual function so that they can continue to protect themselves on the battlefield.

An early success in this program is the demonstration of an exquisitely precise treatment which blockades the specific neurochemical mediator of tissue pain. This treatment has none of the depressant effects of narcotics such as morphine, and may even be utilized as a pain preventative. But what about severe bleeding? With hemorrhage, depletion of vascular volume and red cell mass significantly impairs oxygen delivery to the organs and tissues. Typical medical approaches to treat severe hemorrhage involve attempts to restore the circulation with iv fluids and blood - when and if they are available. This approach can be labeled an oxygen "supply side approach." What we at DSO seek to define is a "demand side approach" by asking the question whether the organ and tissue demand for oxygen can be drastically reduced following injury, so that oxygen supply meets demand even in the face of severe blood loss. A focused goal of this program is to mimic the ability of hibernators, deep-diving aquatic mammals, and other species that use innate mechanisms to decrease the metabolic demand for oxygen under a variety of low supply conditions. We are now determining how to induce this state of low oxygen demand in cells, in tissues, and in organs for periods of up to 6 hours - long enough for a safe evacuation to a specialized medical facility. But even with successes in this realm, blood products will still be needed. However, blood products are extremely difficult to store and move in a battle zone. We believe there are revolutionary new strategies. Using a biochemical approach inspired by invertebrate species which actually dehydrate themselves for prolonged periods, we have already demonstrated effective storage of blood platelets, at room temperature, for over 2 years, with near total maintenance of clotting function. This contrasts sharply to current medical storage standards of 5 days under refrigeration. We are now attempting similar breakthroughs with red blood cells. But what if we could eliminate the need to transport blood products at all, but rather produce them locally, near the battlefield, in a way that would make them usable by everyone? We don't know how to do that yet, but are certainly interested in your ideas. In any discussion of medical technology, one shouldn't forget that medicine is one of the last disciplines to enter the digital age. Naturally the agency that developed the Internet plans to do something about that! Currently, we are engaged in an effort to develop a computational representation of an individual soldier. Essentially, this will be a holographic electronic representation that can be used to augment medical care on and off the battlefield. Once constructed, this "virtual soldier" will provide multiple capabilities, including but not limited to automated, precise assessment of battlefield injuries and optimization of medical or surgical therapeutics.

Despite life-saving improvements in protective gear such as body armor, severe traumatic and thermal injuries - often leading to amputations or other severe disabilities - remain a compelling problem.

Assisting these wounded veterans to return to a normal life is every bit as important as the medical care they receive during battle.

As you heard in the DSO introductory talk, our ability to understand how the brain codes and transmits information can lead to revolutionary new prosthetics.

But there is much more that we are planning to do.

One of the areas we are investigating is accelerated healing. We seek to reduce healing times by 50% , thus minimizing the potential for serious complications like infection and limb atrophy.

Our approach to this problem is to first understand - and then ultimately control - the normal biologic factors that affect the growth of new cells after injury.

While rapid healing from wounds and burns is the early win, thinking long term, it would certainly be a DARPA-hard problem to learn how to actually re-grow severed limbs.

This ability to regenerate limbs is present in many species, and even humans can regenerate a normal liver after removing as much as 90% of it during surgery.

So why can't this regenerative capability be available for human limbs or the brain and spinal cord?

And finally, we believe that DARPA can make a unique contribution to the general health and well being of our soldiers - a contribution that will significantly increase their probability of mission success. We often take for granted that members of the military are healthy when they are deployed.

However, nearly all of their missions involve work in close physical proximity, under stressful and extreme conditions, and in environments filled with pathogens not found in the United States.

Studies, including those done during Special Forces training, have demonstrated such extreme physical and mental exertion can significantly compromise immune function.

Much like marathon runners, who are highly susceptible to illness during a critical interval following their run, soldiers under stressful conditions are very likely to have depressed cellular and humoral immunity and have a high risk of become sick enough to jeopardize military operations.

Our program first seeks to fully understand the behavior of the immune system under these stressful conditions, and then how to regulate the immune system in order prevent susceptibility to disease on the battlefield.

Since the immune system responds to many stimuli - including nutrition, sunlight, and direct innervation from the brain - we are not limiting our options to any particular approach.

But even when we understand the effects of the battlefield environment on the health of the soldier, and learn how to mitigate its consequences, it will be impossible to completely prevent exposure to infectious diseases.

Epidemics like SARS or even common viruses such as influenza can have a devastating effect on mission performance once symptoms appear.

At DSO, we would like to know whether someone will contract a disease before symptoms appear.

Such pre-symptomatic diagnosis is the holy grail of the medical community.

There have been some successes with the examination of breath and blood, but we are still looking for new approaches to find the complex markers that precede the onset of a disease - and please don't limit your thoughts limited to conventional "medical type" measurements, because there are nearly infinite numbers and combinations of physical or mental parameters which are yet unexplored.

The solution set will likely be complex, and therefore we believe that mathematical modeling, particularly modeling which allows biological inferences, will be critical for success.

We believe that the intersection of math and medicine will provide rich rewards, although we do not yet know the exact nature of this synergy. One example is that of epidemiology - the study of diseases and their spread.

We would like to define a new field of epidemiology - "predictive epidemiology", in order to predict the genesis of new diseases - like SARS, HIV, Legionella, or Ebola - before they actually occur. Since we must be able to deploy forces anywhere in the world on a

moment's notice, we are looking for ideas on how to do such predictive epidemiology.

Such prognostic biocomputation will allow unprecedented protection against emerging diseases both for our troops, as well as the rest of the world.

So in closing, let me thank you for the opportunity to share our plan to discover entirely new strategies for maintaining the health, survivability, and peak physical and cognitive performance of the soldier.

The first step is to aggressively raise the bar of expectations, and then put aside conventional paradigms and their artificially imposed limitations.

Then, and only then, will we be able to radically improve warfighters' performance and rehabilitation from injury. We need your ideas to make this happen.

Thank you.