E. NATIONAL SECURITY

THEME E SUMMARY

Panel: R. Asher, D.M. Etter, T. Fainberg, M. Goldblatt, C. Lau, J. Murday, W. Tolles, G. Yonas

The fourth NBIC theme examines the ways in which the United States and modern civilization can meet the intelligence and defense challenges of the new century. In a world where the very nature of warfare is changing rapidly, national defense requires innovative technology that (a) projects power so convincingly that threats to the United States are deterred, (b) eliminates or minimizes the danger to U.S. warfighters from foe or friendly fire, and (c) reduces training costs by more than an order-of-magnitude through augmented reality and virtual reality teaching aids.

Investment in convergent nanotechnology, biotechnology, information technology and cognitive science is expected to result in innovative technologies that revolutionize many domains of conflict and peacekeeping. We are entering an era of network-centric combat and information warfare. Increasingly, combat vehicles will be uninhabited, and robots or other automated systems will take on some of the most hazardous missions. Effective training will make extensive use of augmented or virtual reality. Nanotechnology will offer reliable means for detecting and protecting against chemical and biological agents. Convergence of many technologies will enhance the performance of human warfighters and defenders, in part through monitoring health and instituting prophylaxis, and through magnifying the mental and physical capabilities of personnel.

The Defense Science and Technology Strategy (Department of Defense 2000) seeks to ensure that the warfighters today and tomorrow have superior and affordable technology to support their missions and to give them revolutionary war-winning capabilities. There is special focus on information assurance with emphasis on security; battlespace awareness with emphasis on sensor webs, miniaturized platforms, netted information and cognitive readiness; force protection with emphasis on chemical/biological defense; and support for the warfighter.

In the recent past, new technologies have dramatically enhanced American ability to both prepare for and execute military actions. By implementing advances in information technologies, sensors, and simulation, we have strengthened our ability to plan and conduct military operations, quickly design and produce military systems, and train our forces in more realistic settings. These technologies are central to greater battlefield awareness, enabling our forces to acquire large amounts of information, analyze it quickly, and communicate it to multiple users simultaneously for coordinated and precise action. As former Defense Secretary William J. Perry has noted, these are the technological breakthroughs that are “changing the face of war and how we prepare for war.”

There are numerous special programs, reports and presentations that address these goals. The Department of Defense has designated nanoscience as a strategic research area in order to accelerate the expected benefits (Murday 1999). Various conferences and studies have been devoted to assessing nanotechnology status and needs for defense (Murday 2000; National Research Council, forthcoming). Attention has also been paid to anticipating more global societal consequences of those efforts in support of national security (Roco and Bainbridge 2001).

National Security Goals for NBIC

This conference panel identified seven goals for NBIC augmentation of national security, all of which require the close integration of several of the nanotechnology, biotechnology, information technology, and cognition fields of endeavor. The seven goals, listed below, are sufficiently diverse that there is no common strategy beyond the need for interdisciplinary integration. The net result of accomplishing the stated goals would reduce the likelihood of war by providing an overwhelming U.S. technological advantage, would significantly reduce the cost of training military manpower, and would significantly reduce the number of lives lost during conflict.

i) **Data linkage, threat anticipation, and readiness.** Miniaturized, affordable sensor suites will provide information from previously inaccessible areas; high-speed processing will convert the data into information; and wide-bandwidth communication pipelines with digital security will distribute information rather than data to all who need it.

ii) **Uninhabited combat vehicles.** Automation technology (including miniaturization of sensing, augmented computation and memory, and augmented software capability) will enable us to replace pilots, either fully autonomously or with pilot-in-the-loop, in many dangerous warfighting missions. The uninhabited air vehicle will have an artificial brain that can emulate a skillful fighter pilot in the performance of its missions. Tasks such as take-off, navigation, situation awareness, target identification, and safe return landing will be done autonomously, with the possible exception of circumstances requiring strategic or firing decisions. Without the human g-force constraint and the weight of human physical support equipment (oxygen, ejection system, armor, etc.), the planes will be more maneuverable. Tanks, submarines, and other combat vehicles will experience similar benefits.

iii) **Warfighter education and training.** A partnership between nanotechnology and information technology holds the promise for relatively inexpensive, high-performance teaching aids. One can envision a virtual-reality teaching environment that is tailored to the individual's learning modes, utilizes contexts stimulating to that individual, and reduces any embarrassment over mistakes. The information exchange with the computer can be fully interactive, involving speech, vision, and motion. Nanodevices will be essential to store the variety of necessary information and to process that information in the millisecond time frames necessary for realtime interaction.

iv) **Chemical/biological/radiological/explosive (CBRE) detection and protection.** Microfabricated sensor suites will provide ample, affordable, error-free forewarning of chemical, biological, radiological, or explosive threat. For those who must work in a contaminated environment, individual protection (masks and clothing) will induce heat stresses no greater than conventional uniforms while providing full protection. Decontamination and neutralization procedures will be effective against agents, yet will be relatively benign to people and the environment. Monitors will provide information on warfighter physiological status and initiate any necessary prophylaxis.

v) **Warfighter systems.** The warfighter is subjected to periods of intense stress where life or death decisions must be made with incomplete information available, where the physiology of fatigue and pain cloud reason, and where supplemental technology must compete with the 120 pounds of equipment weight s/he must carry. NBIC technologies can address all of these aspects of warfighting. Nanotechnology holds the promise to provide much greater information, connectivity, and risk reduction to the warfighter. The continued miniaturization of electronic devices will provide 100 times more memory with less bulk and weight (a terabit of information in a cm^2). Processing speeds will increase to terahertz rates. Displays will be flexible and paper-thin, if not replaced by direct write of information on the retina. High-bandwidth communication will be netted. Prolific unattended sensors and uninhabited, automated surveillance vehicles under personal warfighter control will be providing high data streams on local situations. Weapons will automatically track targets and select precise firing times for greater accuracy. The marriage of semiconductors and biology will provide physiological monitors for alertness, chemical or biological agent threats, and casualty assessment. The small size of the nanodevices will limit the volume, weight, and power burdens.

vi) **Non-drug treatments for enhancement of human performance.** Without the use of drugs, the union of nanotechnology and biotechnology may be able to modify human biochemistry to compensate for sleep deprivation and diminished alertness, to enhance physical and psychological performance, and to enhance survivability rates from physical injury.

vii) **Applications of brain-machine interface.** The convergence of all four NBIC fields will give warfighters the ability to control complex entities by sending control actions prior to thoughts (cognition) being fully formed. The intent is to take brain signals (nanotechnology for augmented sensitivity and nonintrusive signal detection) and use them in a control strategy (information technology), and then impart back into the brain the sensation of feedback signals (biotechnology).

Statements and Visions

Defense applications are intended for the highly competitive environments of deterrence, intelligence gathering, and lethal combat, so it is essential to be technologically as far ahead of potential opponents as possible. The United States and its closest allies represent only a small fraction of the world population, and in the asymmetrical conflicts of the early twenty-first century, even a small number of dedicated enemies can cause tremendous damage. Thus, the overview statements and future visions written by participants in the national security working group address very high-priority areas where the United States and its allies can achieve and maintain great superiority. The statements and visions cover areas from enhancing soldier performance (M. Goldblatt) and combat readiness (D.M. Etter) to future roles of NBIC for fighting terrorism (J. Murday, T. Fainberg, C. Lau) and equipment of soldiers (R. Asher, J. Murday, T. Fainberg, C. Lau).

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STATEMENTS

COGNITIVE READINESS: AN IMPORTANT RESEARCH FOCUS FOR NATIONAL SECURITY

Delores M. Etter, United States Naval Academy

Cognitive readiness is a critical research area for the Department of Defense. Soldiers must not only be ready physically for the myriad of roles that they have in the world today, but they must also be ready cognitively. This cognitive readiness extends from handling stress and sleep deprivation, through training "anytime, anyplace," through additional information provided by augmented reality, and through realtime physical monitoring during operations. This range of cognitive readiness requires a serious investment in research covering a wide range of areas. This paper will present some of the focus of existing research and some of the paths for future research in this area as it applies to national security.

Critical Focus Areas for DOD S&T

Approximately three years ago the senior directors in the Office of the Deputy Under Secretary of Defense for Science and Technology selected five areas as especially critical areas in DOD's research program. These five research areas are the following: chemical and biological defense, hardened and deeply buried targets, information assurance, smart sensor web, and cognitive readiness. Today, these five areas seem to be obvious priorities, but three years ago that was not the case. These areas had existing research programs that were supported by the military service research programs and the defense agencies. The identification of these five areas by the Office of the Secretary of Defense gave these areas a corporate priority. Additional funds were provided to start new programs, coordinate existing programs, and to support workshops to bring together new players who worked in various aspects of the areas.

The Department's focus on chemical and biological defense has been a clear priority for DOD over the last few years. The need for this research results from proliferation of inexpensive weapons of both chemical and biological agents. DOD's research has four key areas of priority: detection of the agents, protection from the agents, decontamination of equipment and people after exposure, and an understanding of the dispersion of the agents from a modeling and simulation perspective.

Concern over hardened and deeply buried targets comes from the fact that underground facilities are often used to conceal missiles and weapons of mass destruction. DOD's research program includes priorities in overhead imagery to attempt to locate the targets, sensor research to determine what activities are being carried out underground, delivery systems to neutralize facilities if necessary, and computational modeling activities to understand the structures and activities within them.

Cyberterrorism is a real part of today's world. Attacks come from hackers, terrorists, and from insiders. Dealing with information warfare is critical to assure that our information is protected and is not compromised. Research in information assurance involves designs of new firewalls, malicious code detectors, encryption techniques, and correlation technologies.

Smart sensor web is a concept that provides complete situation awareness to the individual soldier in the field. It is based on integrating information from areas such as realtime imagery, micro weather information, and moving targets. The research includes physical model understanding, dynamic data bases, microsensors, wireless communications, and the next-generation Internet.

Cognitive readiness addresses human optimization. The challenges to the human include sustained operations, environmental ambiguity, and information overload. Research programs address topics such as physiological monitoring, embedded training, learner-centric instruction, and augmented reality. Figure E.1 shows the wide range of areas covered by cognitive readiness.

Figure E.1. Cognitive readiness research.

Cognitive Readiness Framework

The DOD has a multidisciplinary focus on the human dimension of joint warfighting capabilities. This cross-Service framework ensures that research addresses the following requirements:

- warfighters are mentally prepared for accomplishing their missions
- warfighters are performing at their optimum
- tools and techniques for preparing warfighters are the most effective and affordable
- tools and techniques that warfighters use are the most effective and affordable

The changing military environment compels a focus on cognitive readiness. Issues that affect this aspect of military readiness come from many directions. Soldiers have many different threats and changing missions that extend from peacekeeping to warfighting. Budget reduction brings personnel drawdowns in the military, and that brings demographic changes. In addition, military systems are becoming more complex, and soldiers need to handle new technologies. Figure E.2 illustrates the range of these interactions that soldiers must handle.

Figure E.2. Changing military environment.

Four domains from science and technology research have been defined for cognitive readiness:

- *Sociology and personnel*. This domain deals with family, group and culturally defined issues, selection and classification, and leadership.

- *Health and welfare*. This domain includes mental acuity, fatigue, physiological readiness, quality of life, and morale.

- *Human systems integration*. This domain covers human-centered design, decision aids, and dynamic function allocation.

- *Education and training*. This domain includes using new technologies for teaching/learning and to develop specific tasks, skills, and/or procedures.

The following three examples demonstrate the wide range of research necessary to support cognitive readiness. *Augmented reality* involves bringing the information world to the soldier in real time. *Biomedical monitoring* combines sensors for measuring the physical readiness of soldiers to real time monitoring to judge performance capability. *Survival technologies* present different areas of research to protect soldiers physically so that they are mentally and physically ready to perform their missions.

Example 1: Augmented Reality

Consider an urban environment. Soldiers need to know immediate answers to questions such as

- How do I get to this building?

- What building is in front of me?

- Where is the main electric circuit in this building?
- What is the safest route to this building?
- Are there hidden tunnels under the streets?
- Street signs are missing – where am I?
- Have sniper locations been identified?

The area of augmented reality is an area in which technology is used to augment, or add, information for the soldier. For example, augmented reality could amplify natural vision by projecting information on a soldier's visor, or perhaps projecting it directly on the soldier's retina. This additional information added to the natural view could identify warnings for sniper locations and mines. Hidden infrastructure and utilities such as subways, service tunnels, and floor plans could be displayed. Virtual information such as simulated forces could be displayed to provide new training simulations. Figure E.3 gives an example of the type of information that would be very helpful if it were shown over an image to augment the information available to a soldier.

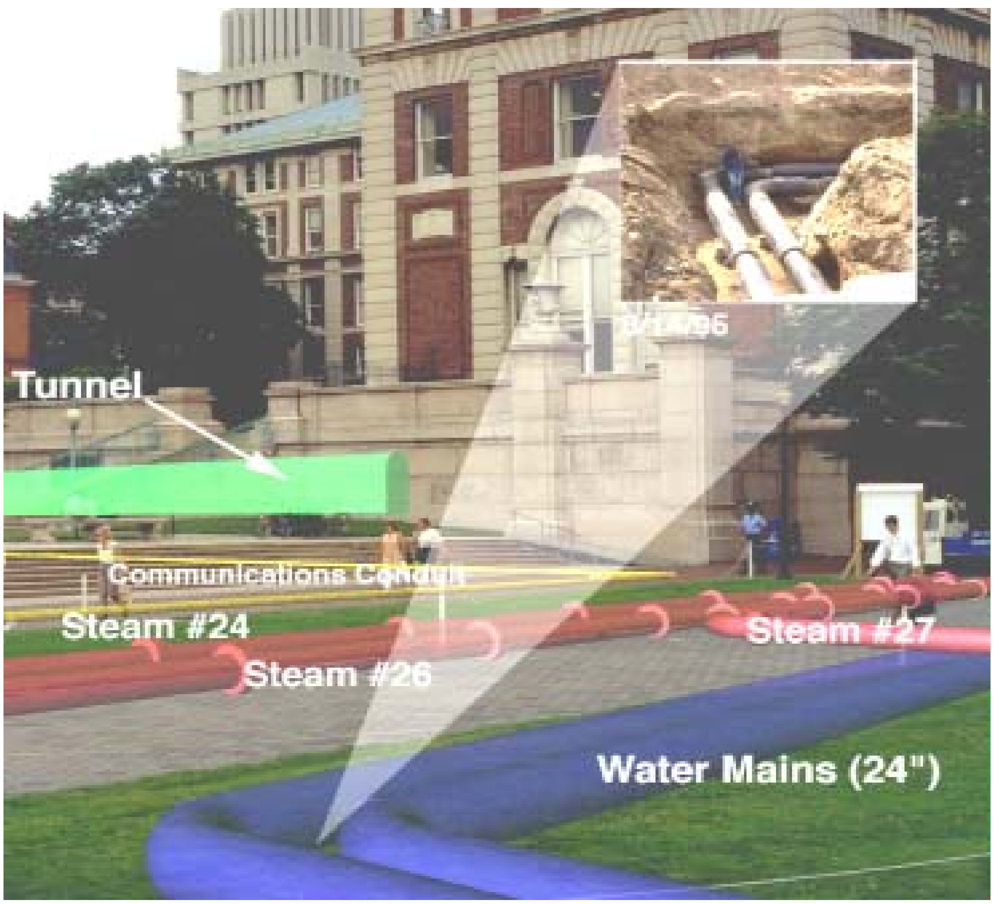

Figure E.3. Augmented reality.

Example 2: Biomedical Status

Biomedical status monitoring is the medical equivalent of the Global Positioning System (GPS). It uses sensors for vital signs, electrolytes, stress hormones, neurotransmitter levels, and physical activity. In essence, it locates the soldier in physiological space as GPS does in geographic space.

The biomedical status monitoring program is integrated into several DOD programs, including Land Warrior, Warrior's Medic, and Warfighter Status Monitor. These programs allow dynamic operational planning with biomedical input that supports pacing of operations at sustainable tempo. It also allows commanders to anticipate and prevent casualties due to heat stress, dehydration, performance failures from sleep deprivation, and combat stress casualties. Not only can casualties be detected, but initial treatment can be guided.

Figure E.4 gives an example of a wrist monitor that predicts performance by monitoring sleep. Sleep is determined by the lack of motion of the wrist monitor. The graph in the figure predicts performance based on the amount of rest that the soldier has had.

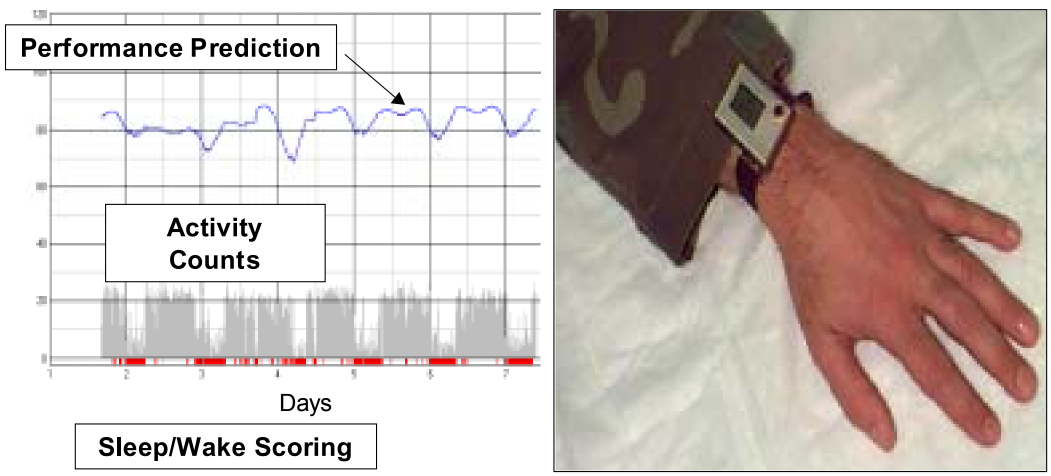

Figure E.4. Sustaining performance: managing sleep.

Sensors can also help prevent casualties by monitoring soldiers in MOPP gear – the equipment worn to work in hazardous environments. The sensors can include core temperature (collected from a sensor that is swallowed by the soldier), skin temperature, heart rate, and activity rate. The combination of these sensors can be used to determine when a soldier needs to take a break in order to prevent possible injury or death.

Figure E.5 illustrates the hypothetical use of these biomedical status monitoring devices when they are combined with wireless communication systems. Individual soldier status can be monitored not only by soldiers working side by side, but also by central units that can be mobile or transmitted to satellite systems. Future sensors may also be embedded bionic chips.

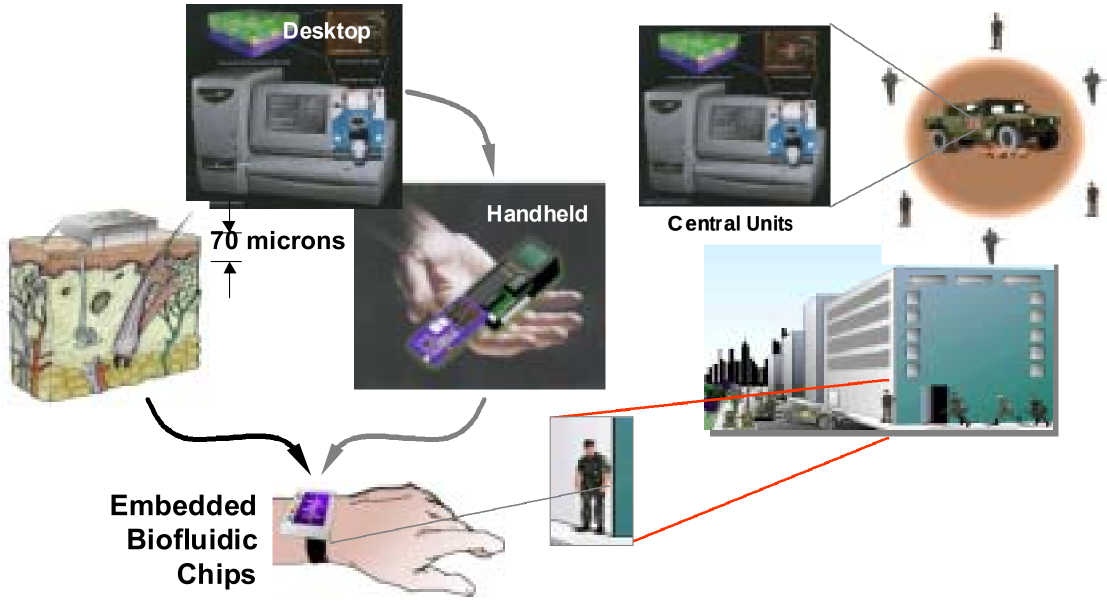

Figure E.5. Wrist-mounted remote biological assay.

Example 3: Survival Technologies

A number of new survival technologies are being developed to provide human protection in a number of different ways. Ballistics protection, shown in Figure E.6, is being studied using new high-performance fibers, composite materials, advanced ceramics, and metals. The analysis of new materials requires enhanced predictive modeling of the effects of ballistic weapons with these new materials. Another challenge is integrating the new materials into uniform systems.

Figure E.6. Ballistics protection.

Innovative research in chemical/biological protection for soldiers is investigating selectively permeable membranes that would provide an outer coating for uniforms. The coating would not allow aerosols or liquids to penetrate from the outside of the material. Additional research is being done in elastomeric protective materials and lightweight carbonless materials. A diagram showing some of the interactions between various layers of the material is shown in Figure E.7.

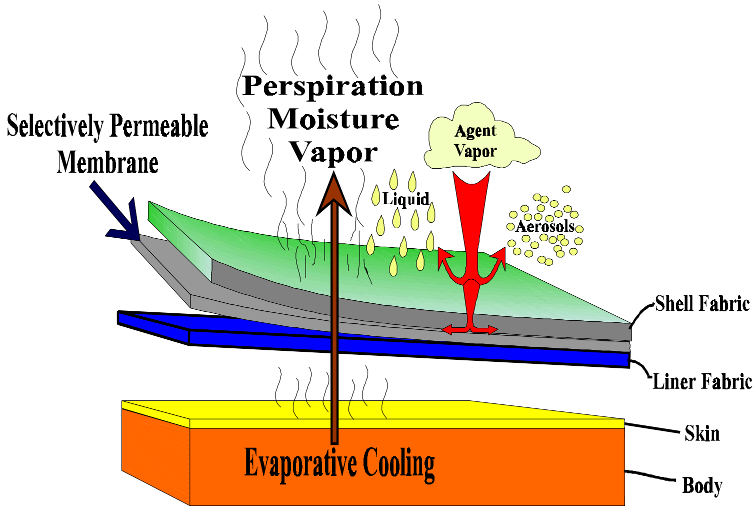

Figure E.7. Selectively permeable membranes for uniforms.

Directed-energy eye protection (protection from lasers) is a challenge because of the various frequencies of lasers. Some current systems are considering robust dielectric stacks on polycarbonate, enhanced-eye-centered holograms, operational dye technology, and nonlinear optical effects.

New materials are providing possibilities for multifunctional materials. Examples include aramid co-polymer chemistry and flame-retardant chemistry. Some of the possibilities for microencapsulation may provide phase-change materials — materials that change to match the environment of the soldier. This would provide a chameleon-like uniform.

Finally, systems integration will play an important part of combining many of the new capabilities such as microelectronics, improved lightweight sensors, and advanced materials. The work on high-resolution flat panel displays will provide wearable computer screens, and that will significantly reduce the weight of equipment that soldiers need to carry.

Conclusions

This article has briefly provided some of the reasons why cognitive readiness is such an important area to national security and identified some of the research that is being supported in this area. Successful research will require research partnerships that bring together researchers from universities, government agencies, industry, and international coalitions. The benefits have far ranging possibilities that will address cognitive readiness not only of soldiers, but of general populations as well.

Acknowledgements

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DARPA'S PROGRAMS IN ENHANCING HUMAN PERFORMANCE

Michael Goldblatt, Defense Advanced Research Projects Agency

The Defense Advanced Research Projects Agency (DARPA) was established in 1958 as the first U.S. response to the Soviet launching of Sputnik. Since that time, DARPA's mission has been to assure that the United States maintains a lead in applying state-of-the-art technology for military capabilities and to prevent technological surprise from her adversaries.

With the infusion of technology into the modern theater of war, the human has become the weakest link, both physiologically and cognitively. Recognizing this vulnerability, DARPA has recently begun to explore augmenting human performance to increase the lethality and effectiveness of the warfighter by providing for super physiological and cognitive capabilities.

Metabolic Engineering

The Metabolic Engineering Program seeks to develop the technological basis for controlling metabolic demands in cells, tissues, and organisms. The initial phase of the program is focusing on the successful stabilization and recovery of cells and tissues from stress states representative of military operational conditions, with specific focus on blood and blood products (Fig. E.8).

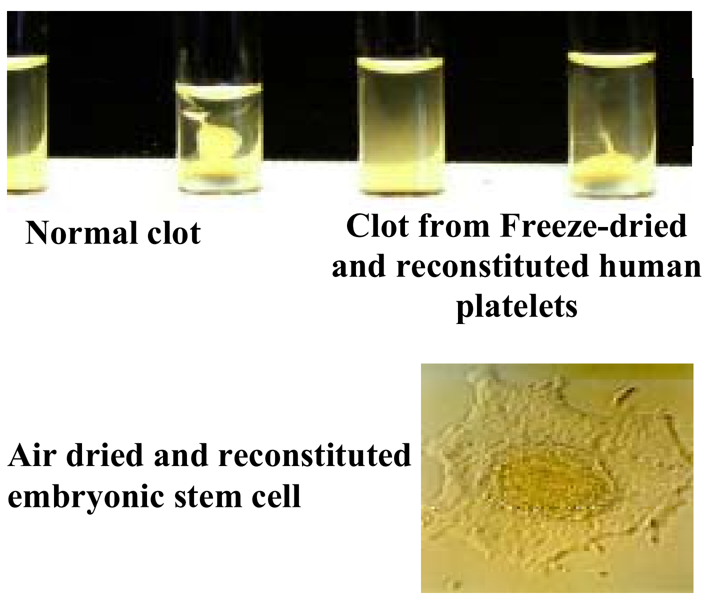

Figure E.8. Develop methods for controlled metabolism in cells, tissues, organs, and organisms needed by the U.S. military population.

When successful, the application of this technology to combat casualties will result in greater salvage of human life and limb from the battlefield, through the availability of cell-based therapy for hemorrhage, shock, and critical wounds. Additionally, stabilized cells and tissues will provide a stable substrate for prepositioning and large-scale manufacture of needed cellular and tissue products.

Exoskeletons for Human Performance Augmentation

The goal of the human performance augmentation effort is to increase the speed, strength, and endurance of soldiers in combat environments. The program will develop technologies, such as actively controlled exoskeletons, to enable soldiers to handle more firepower, wear more ballistic protection, and carry more ammunition and supplies, etc., in order to increase the lethality and survivability of ground forces in all combat environments (Fig. E.9).

ISMSñRobot Supporting Human

Motion Capture System

Figure E.9. Incorporate and advance technologies to remove the burden of mass (120+ lbs.) and increase the soldier's strength, speed, endurance, and overall combat effectiveness.

Two of the critical issues for exoskeletons are power for actuation and biomechanical control integration. The program is developing efficient, integrated power and actuation components to generate systems with duration that are operationally significant. Hence, researchers are exploring the use of chemical/hydrocarbon fuels (with very high energy density and specific energy) for energy conversion and mechanical actuation (as opposed to other energy storage media such as batteries or compressed air). An understanding of biomechanics, feedback, and control are also critical to building an integrated system that provides seamless compatibility with human kinetics, especially under battlefield stress.

Augmented Cognition

The DARPA Augmented Cognition program promises to develop technologies capable of extending the information management capacity of warfighters. This knowledge empowerment will be accomplished in part by exploiting the growth of computer and communication science and accelerating the production of novel concepts in human-computer integration (Fig. E.10).

The mission of the Augmented Cognition program is develop and demonstrate quantifiable enhancements to human cognitive ability in diverse, stressful, operational environments. Specifically, this program will measure its success by its ability to enable a single individual to successfully accomplish the functions currently carried out by three or more individuals.

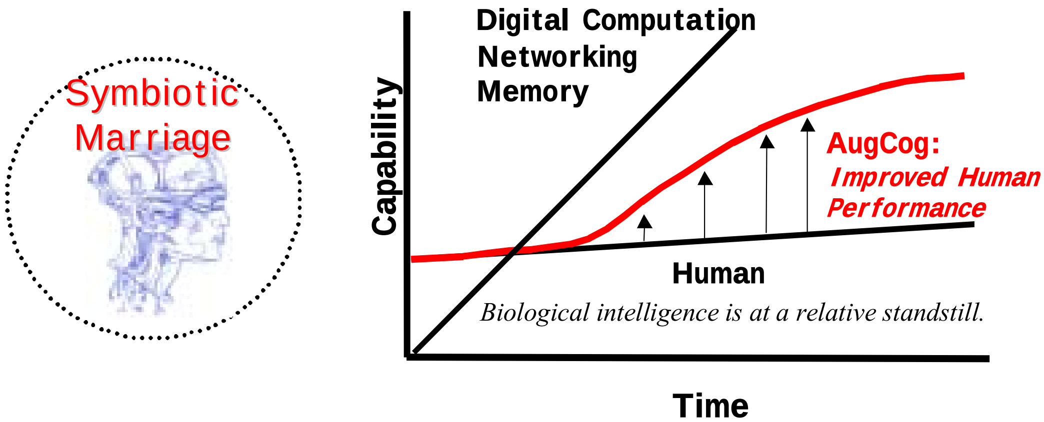

Figure E.10. Maintain a person's cognitive state at an optimal arousal level, then the person will have enhanced memory and the ability to perform optimally even under conditions of interruptions; this will improve and enhance the quality of military decisionmaking.

The program will explore the interaction of cognitive, perceptual, neurological, and digital domains to develop improved performance application concepts. Success will improve the way twenty-first century warriors interact with computer-based systems, advance systems design methodologies, and fundamentally reengineer military decisionmaking.

Continuous Assisted Performance (CAP)

The goal of this program is to discover new pharmacologic and training approaches that will lead to an extension in the individual warfighter's cognitive performance capability by at least 96 hours and potentially for more than 168 hours without sleep. The capability to resist the mental and physiological effects of sleep deprivation will fundamentally change current military concepts of "operational tempo" and contemporary orders of battle for the military services.

The program will develop a number of different pharmacologic approaches using animal models (Fig. E.11) to prevent the effects of sleep deprivation over an extended period of time, nominally set at up to 7 days. At the end of the program, we expect several candidate drugs that alone, or in combination, extend the performance envelope.

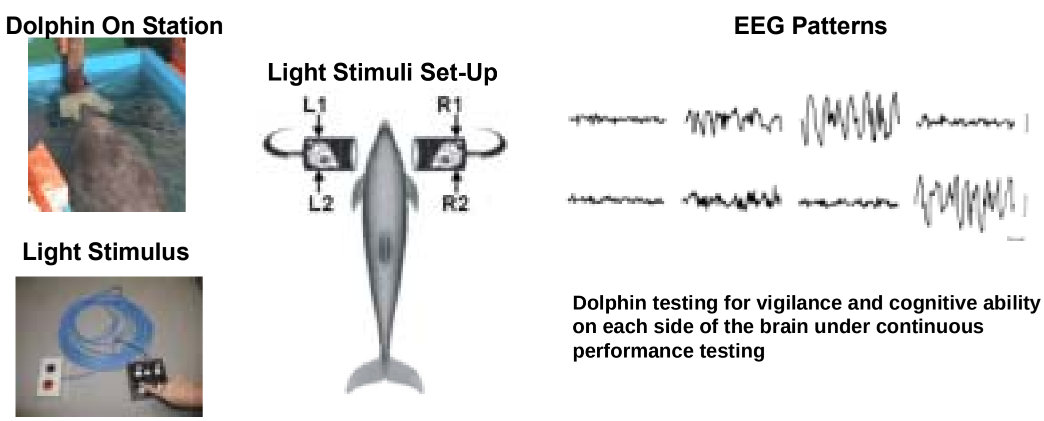

Figure E.11. Develop multifaceted approaches to prevent the degradation of cognitive performance caused by sleep deprivation in order to extend personnel "duty cycle."

A minimum of four different approaches will be the core of the CAP program:

1. Prevent the fundamental changes in receptor systems of the information input circuits caused by sleep deprivation.

viii) Discover the system that causes a reset of the network during sleep and develop a drug that activates this process in the absence of sleep.

ix) Stimulate the normal neurogenesis process that is part of learning and memory, thereby increasing the reserve capacity of the memory circuits.

x) Determine if individuals resistant to sleep deprivation use a different strategy in solving problems and, if so, then develop a training approach that makes this possible for everyone.

Brain-Machine Interface

This program uses brain-machine interfaces to explore augmenting human performance by extracting neural codes for integrating and controlling peripheral devices and systems. The program attacks the technological challenges across many disciplines and will require assembly of interdisciplinary teams to achieve the ambitious goal of having humans interact with and control machines directly from brain activity.

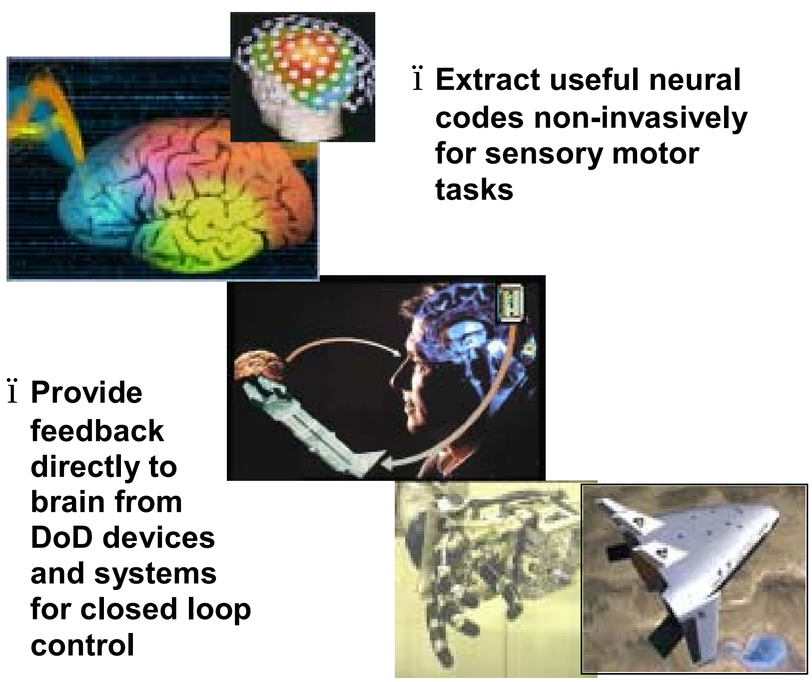

Figure E.12. Augment human performance by harnessing brain activity to command, control, actuate, and communicate with the world directly through brain integration and control of peripheral devices and systems.

Three of the significant challenges that the program will explore are

2. fundamental extraction of patterns of neuronal code as they relate to motor activity and the proprioceptive feedback necessary for executing motor commands

xi) non-invasive access to the necessary brain activity (access a 500 micron square area where temporal spike train outputs can be measured)

xii) design and fabrication of new machines (elasticity, compliance, force dynamics) that could be optimally controlled by the brain.

NBIC for Homeland Defense: Chemical / Biological / Radiological / Explosive (CBRE) Detection/Protection

James Murday, Naval Research Laboratory

The coupling of nanoscale sensors for chemical/biological/radiological/explosive protection (CBRE) with improvements in information technology and physiology can critically impact national security programs by providing sensitive, selective, and inexpensive sensor systems that can be deployed for advance security to the following kinds of locations:

- transportation modes (security protection for air, bus, train/subway, etc.)
- military (for protection of facilities and equipment)
- federal buildings (government offices, U.S. Embassies, all other federal buildings)
- U.S. Customs (for border crossings, international travel, etc.)
- civilian businesses (in large and small cities)
- the environment (public water supplies, waste treatment plants, natural resource areas, reservoirs, etc.)
- schools (to prevent weapons, explosives such as pipe bombs, etc.)

Improvements in detection systems, coupled with new approaches to protection, promise potential impact that is vast and critical.

Role of Converging Technologies

Converging NBIC technologies will integrate the biology, chemistry, electronics, engineering, materials, and physics research communities to establish the interdisciplinary nanoscience knowledge and expertise needed to exploit nanofabrication and nanostructures in the development of

- miniaturized, intelligent sensor systems with revolutionary CBRE performance
- new high-surface-area, templated adsorbents for personnel/collective protection systems
- nanofibers for effective clothing with minimal heat loading
- catalytic materials effective against agent while relatively benign to humans and environment
- mechanisms to disrupt biological agent viability

Nanotechnology will provide innovative new hardware. Information technology will provide the effective transformation of new data into information. Biotechnology will provide new insights into human physiology and prophylaxes. Together, these three technologies can lead to effective new protection systems against the CBRE weapons of mass destruction.

Transforming Strategy to Reach Vision

Short-Term (1-5-Year) Transition Opportunities

To be successful in the 1-5-year timeframe, opportunities must have already demonstrated proof-of-principle and have existing commercial interest. Specific examples include those shown in Table E.1.

. Examples of Commercialized Nanotechnologies

Investigator	Institute	Technology	Company
Mirkin	Northwestern	nanoAu biological sensing	Nanosphere, Inc.
Lieber	Harvard	nanotube sensors	Nanosys
Snow	NRL	nanoAu chemical sensing	MicroSensor Systems
Klabunde	Kansas State	nanocluster agent catalysis	Nanoscale Materials
Thundat	ORNL	cantilever bio/chem sensing	Protiveris
Smalley	Rice	CNT for adsorbents	CTI
Doshi		polymer nanofibers	eSpin

SBIR and STTR funding can accelerate the transformation of the existing science discovery into technology ready for commercial attention.

Mid-term (5-10-Year) Transition Opportunities

Those areas where an investment in nanoscience holds the promise for paradigm-breaking approaches to detection/protection/neutralization with commercial product transition in the 5-10 year timeframe include the following:

Sensing

- transduction/actuation mechanisms for greater sensitivity/selectivity
- biotic/abiotic interfaces to marry semiconductors with in-vivo biology
- environmental energy sources to minimize battery requirements

Protection

- high-surface-area materials with templated structure for selective adsorption
  - controlled porosity for separation
  - nanofibers for clothing with improved adsorption/neutralization of agent
- neutralization/decontamination
  - nanostructures to disrupt biological function
  - catalytic nanostructures
- Therapeutics
  - Encapsulated drugs for targeted release

– MEMS "capsules" for controlled drug release

Long-Term (10-20-Year) Transition Opportunities

Investment in the science base long-term is believed to be important for ultimate integration of many components into a complex system (e.g., sensor suites) and for providing sufficient insights into a complex system (e.g., cell and spore physiology) to enable innovative technologies. Examples include

- Laboratory on a chip — incorporation of multiple separation and detection technologies at sub-micron scales on a single chip in order to obtain inexpensive, rapid detection technology with low false positive/negative events
- Cell-based sensing — development of sensing technology that responds to unknown new threats by measuring the response of living systems that can mimic human biochemistry
- Nanoelectromechanical systems (NEMS) — extension of the MEMS technologies another three orders smaller in order to incorporate significantly more capability

Estimated Implications

Since the United States presently can dominate any military confrontation, it is highly likely that the nation will continue to suffer from terrorist actions such as the World Trade Center and the subsequent anthrax distribution. The application of convergent technologies to national defense has the potential for revolutionary new capability to counter the threats.

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FUTURE ROLES FOR SCIENCE AND TECHNOLOGY IN COUNTERTERRORISM

Tony Fainberg, Defense Threat Reduction Agency, Department of Defense

The natural reaction among scientists, engineers, and technical experts following the atrocities of September 11 was the fervent wish to apply their knowledge, abilities, and creativity in order to contribute to the defeat of current and future terrorist threats to the United States and its international friends and allies.

Indeed, there is ample opportunity for directing technical advances to this end. However, it should be emphasized that much can be accomplished nearly independently of technical innovations. Security procedures need to be improved in many venues. The most talked-about area today is aviation security; for example, the need to know who has access to airplanes at airports is pressing. Background checks to this end are now being instituted, and, although enabled by advances in computer technologies of various sorts, can already be accomplished, given bureaucratic acquiescence. But although technical applications can enable these checks, the main barriers to doing so in the past have been cost, inconvenience, and concerns about intrusion on privacy. Another example is in the area of explosives detection. Excellent equipment for detecting explosives in baggage has been developed and manufactured as long ago as 1994. Since 1997, this equipment has been deployed and further developed, but it could be deployed in such a way as to cover the whole civil aviation system rather than just 10 percent of it. Under the current, new imperatives, these and a number of other matters can and will be resolved through national resolve rather than advanced technology. Especially for the near-term, there is much that can be done to reduce our vulnerabilities (indeed, much is being done), without developing a lot that is new in the way of science and technology.

But, although science and technology are not the only answers to the diverse and menacing terrorist threat, they are part of the answer and will increasingly become so in the future. New integrated systems and approaches will be necessary both to increase the robustness of our society against bioattacks and to face newer threats, which themselves may be developed through the use of science and technology.

I will try to lay out some thoughts about where we might conceivably look for new tools to deal with threats that have occurred or that we can easily imagine occurring. My emphasis is on technologies that could begin to produce useful results in the mid-term (say, 2-3 years to 10 years), particularly those areas that are within the scope of this workshop's focus on the convergence of nanoscience/ nanotechnology, biotechnology/biomedicine, information technologies, and cognitive science.

Aviation Security[1]

One main problem in the area of aviation security that might be addressed by some of the NBIC technologies would be trying to find out (a) who the people are who have access to aircraft and (b) what their intentions are.

A second problem lies in the timely detection of chemical or biological agents, particularly in airports, and in what to do about the alarms, false and real. Chemical detectors are fairly good right now, although like everything else, they can be improved, especially regarding false alarms. One does need to program them to look for the particular agents of interest. The issues then are cost, where to deploy, and how to deal with false alarms. I will touch more on biosensors in the following section.

Infotech is the technical key to determining who the people are who have access to aircraft, and it also offers the first clues to their intentions. The people with access are those who work at airports, including screeners, and the passengers and crew. One problem is to distill information from various databases, most domestic, some international, to ferret out those individuals who are known or suspected to be threats. There will be a resistance to sharing from those possessing the information on highly sensitive databases. At the minimum, a means must be found for providing only the essential information to the parties controlling access to the aircraft.

Biometrics, including facial recognition technologies, can in principle provide an additional identification tool, beyond the usual name, a minimal amount of personal data, and, perhaps, a picture. However, none of this is any use unless one has the individual of concern in one's database already. In the case of the 19 hijackers, from publicly available information, only three would have triggered any sort of alert. These were due to overstaying visas or having had minor run-ins with the law.

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[1] For comparison with current work, the research and development plans for aviation security within the Federal Aviation Administration may be downloaded from the site, http://www.faa.gov/asd/red98.htm.

For those with access to aircraft, a serious background check needs to access databases that go back longer than a few months or even years: I would assert that it is necessary to track someone's credentials for eight years or more to get a clear enough picture of their potential for criminal conduct. And one constantly needs to verify that those granted access are actually the ones who have been approved for access. We don't want access given to someone who steals an ID, for example. Here, too, infotech and biometrics can only help with part (a substantial part, true) of the job. Procedural security changes are required to protect the civil aviation system adequately from the "insider" threat.

Regarding those who actually board a flight, it would be nice to know whether they have malevolent intentions that pose a risk to others. This is where some technological futurism might possibly be of use. Remote detection of heart rate, adrenaline on the skin, and perhaps other chemicals connected with the "fight or flight" reaction, is imaginable, and some efforts have been proceeding in these areas for years. Voice stress analysis is another possibility, although to my knowledge, there are no highly convincing data that this would provide a reliable trigger for the purposes considered here. And, in the neurological/cognitive realm, on an even more futuristic note, would there be clues one could obtain from a remote (at a meter or two) electroencephalogram that would be useful?

I am somewhat skeptical of all of these possibilities, but the problem is serious enough, in my view, to justify some work in these areas. At the least, one could easily imagine useful by-products for public health and neurological research. Experimental data are needed to learn how reliable (if at all) such indicators would be in a civil aviation context. The obvious issues of effectiveness, false positives, and false negatives will be determinant: a simple demonstration of some vague effect is insufficient.

One needs to bear in mind that the consequences for an individual of triggering the system may not necessary be immediate incarceration for life. A trigger may simply indicate the need to examine carefully just what the individual has brought onto the plane. One might also want to correlate alarms from different individuals on the same flight. False positives, while they need to be controlled, can be tolerated at a moderately low level (say, less than a percent).

Information technologies could obviously be applied to the issue of monitoring or controlling a hijacked plane automatically or from the ground, as has been discussed openly in the press. All this is feasible with current processing, communications, and information technologies and appears to need little further in new research. Whether this approach (especially controlling flight) is a good idea or not, is a further question. Pilots tend to think it is not.

Biodefenses

Sensors[3] *(Refs)*

It would be useful if highly sensitive, specific, broad-spectrum sensors, capable of detecting biological or chemical agents before they could threaten human life, were placed in many environments: transportation nodes, vehicles, public buildings, even homes. They should also be rapid (seconds to a few minutes at the most), and have manageable false alarm rates. What is manageable in this case is rather less than what is manageable in controlling airplane boarding. A false alarm rate of one per year per detector might be barely manageable in some contexts, unless one has the ability to run quick

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[3] Descriptions of government research and development work in chemical and biological detectors may be found in U.S. Department of Energy, *Chemical and Biological National Security Program, FY00 Annual Report* (Washington, DC: U.S. Department of Energy 2000) and U.S. Department of Defense, *Nuclear /Biological/ Chemical (NBC) Defense, Annual Report to Congress,* (Washington, DC: U.S. Department of Defense 2000).

follow-up tests for verification. Even considering only public buildings, probably the most likely civilian target category for attack, the problem is still extremely challenging.

Biotechnology and nanotechnology (or, at least, microtechnology) converge here. There have been efforts in this area for years. I refer particularly to the "lab-on-a-chip" concept, which is being developed and used by national laboratories and private companies. For the purpose of protecting against terrorism (and serious work is going on in this area), one may envision arrays of perhaps up to 1000 by 1000 sites on a small chip, each one populated by a DNA sample from a particular pathogen. If one can sample well enough and devise a PCR process to be fast enough, one might imagine that highly specific detection would be possible. The rub is the time required: current prototypes that do DNA analysis typically require on the order of an hour to process a sample and have a rather small number of pathogens to which they are sensitive. The hope is to reduce this time to minutes or less.

If major improvements in biosensors are, indeed, possible within a few years, the applications in the public health arena are easy to imagine. If a national medical surveillance network is assembled, as some researchers envision (notable among them, Alan Zellicoff of Sandia) and many advocate, the use of an even broader pathogen-detection chip (if cheap enough) could have enormous benefits, both for monitoring and for individual treatment. The spin-offs would more than justify the expense incurred in the main counterterrorist thrust. This is an area I consider extremely fertile for more research and development, perhaps more than any other in the counterterrorist field, and one that needs even more attention than it is currently receiving.

Decontamination

Sensors would have obvious uses for decontamination after an attack. But what about decontaminating the air in buildings? There are current technologies that could be useful, as a matter of course, in buildings with high levels of circulation. Ultraviolet radiation, electron discharges, and nuclear radiation all come to mind as possibilities. As retrofits to current buildings, the cost would generally be prohibitive except for high-value targets. But if reasonably costed options were feasible, new buildings could incorporate such measures. This is an engineering issue and one that I suggest is worthy of some study.

Vaccines and Therapeutics

Vaccines and therapeutics are areas that have, of course, been pursued for a long time: centuries, in fact. Nowadays, the terrorist threat gives new impetus to these pursuits. Especially regarding vaccines, the lack of a strong market has made the large drug companies uninterested in working very hard in this area, and I assert that there is therefore a major role for the government.

A major new field is antiviral drugs, which is highly relevant to terrorism, since many putative agents, from smallpox to the hemorrhagic fevers, are viruses. To an outsider, this looks like a burgeoning subject of study, one poised on the cusp of serious breakthroughs. Major efforts need to be placed here. In this field of bioresearch, as well as many others, the stimulation of work for counterterrorist or defense ends will have many spin-offs for public health that are perhaps more valuable than the original purpose of the work.

Another approach is to look for methods to counter the chemistry and mechanics of infections, to look for commonalities in the way that different agents wreak havoc on multicellular organisms, and to counter the pathogen attack in a generic way. The Department of Energy, DARPA, and, indeed the whole field of microbiology actively work these areas of research. To an outside observer, again, the approach seems intriguing and promising. What I would suggest here is coordination of such work that particularly applies to microorganisms of interest as agents of bioattacks.

A totally different field that has received some attention lately, but probably not enough, is the area of edible vaccines.[4] Synthetically coding for receptor sites on the protein coats of pathogens, and then inserting these DNA strings into a plant genome has produced interesting early results. Workers at the Boyce-Thompson Plant Research Institute at Cornell, in collaboration with researchers at Baylor University, have found immune response in human subjects generated by eating the potatoes that result from such genetic manipulation. Since we have experienced such difficulties in producing a vaccine in large quantity just for anthrax, a totally different path might be in order. Side effects should be minimized by this technique. One could even imagine, eventually, a cocktail, a V-8, of tomatoes, bananas, or some other food, bred to protect against a variety of pathogens. The doses could be easily distributed and delivered, and, in remote or poor areas, would need a minimum of refrigeration and require no needles. Possibly, none of this will work out: maybe the required doses of food will just be too great or will have to be re-administered too often to be practical. But, it seems to me that this is interesting enough to investigate with more vigor than is currently the case.

Other Areas

Time and space severely limit what can be described in an extremely short paper. I will just touch upon other areas that appear to me to be important in combating terrorism. All would involve nanotechnologies and information sciences, falling under the NBIC rubric, since they would probably require advances in computing power to be most effective.

One can try to apply information technology and social sciences in an effort to discern patterns of behaviors in nasty organizations. If one were to focus on correlating a large volume of diverse data that include the characteristics, motivations, and actions, could one achieve any predictive value? Predicting a specific event at a specific time is clearly unlikely, but perhaps a result could be generalized cues that would enable intelligence services to look more closely at a given time at a given group. DARPA is pursuing such avenues, as are, no doubt, other branches of the government.[5] I would not call this cognition per se, but this type of effort does try to encompass, in part through behavioral sciences, how certain types of people might think in specific situations.

Finally, I would like to point to the issue of integrating architectures, applied to many counterterrorist areas. This, too, involves cognition and information science and technology. As a simple example, the security at an airport would greatly benefit from some integration of all the security activities that go on there, including alarms, alarm resolution, personnel assignments, equipment status, and so on.

On a much more complex level, the response to a major terrorist act, involving weapons of mass destruction, would benefit enormously from a generalized C4ISR (command, communications, control, computers, information, surveillance, and reconnaissance) architecture. How does one put the response all together, among so many federal, state, and local agencies? How does urgent information get down to the street quickly and accurately? How is it shared rapidly among all those who urgently need to know? How does one communicate most effectively to inform the public and elicit the most productive public reaction to events? How can one best guide the decisions of high-level decisionmakers in responding effectively to the attack? How are their decisions most effectively implemented? True, we can always muddle through; we always have. But a comprehensive architecture for emergency response could make an enormous difference in how well the society will respond and minimize casualties. And cognitive science and information technology together could

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[4] http://www.sciam.com/2000/0900issue/0900langridge.html, also in *Scientific American*, Sept. 2000.

[5] http://schafercorp-ballston.com/wae/, accessed last on 27 December 2001, contains a description of a DARPA project entitled Wargaming the Asymmetric Environment.

greatly help in devising such architectures. Much talk and much work is proceeding in this area, especially in the past two months. My impression, however, is that some new thinking by newcomers to the counterterrorist field — who have the expertise in operations research, information technology, and cognitive sciences — would be highly productive.

NANOTECHNOLOGY AND THE DEPARTMENT OF DEFENSE

Clifford Lau, Office of the Deputy Under Secretary of Defense for Research

The Department of Defense (DOD) recognized the importance of nanotechnology well before the National Nanotechnology Initiative (NNI). DOD investment in nanoscience dated back to the early 1980s when the research sponsored by DOD began to approach the nanometer regime. Nanoscience and nanotechnology is one of six research areas identified by DOD as strategically important research areas. After careful evaluation and coordination with other federal agencies within the Interagency Working Group on Nanotechnology, the DOD investment was organized to focus on three nanotechnology areas of critical importance to DOD: Nanomaterials by Design, Nano-Electronics/Magnetics/Optoelectronics, and Nanobiodevices. DOD has traditionally provided leadership in nanotechnology research, particularly in the areas of nanoelectronics, chemistry, and materials. The research sponsored by DOD will provide the scientific foundation for developing the nanotechnology to enhance our warfighting capabilities.

DOD Impact

It is anticipated that nanotechnology would impact practically all arenas of warfighting in DOD, including command, control, communications, computers, intelligence, surveillance, and reconnaissance (C4ISR). In addition to providing much greater capability in computing power, sensors, and information processing, nanotechnology will also save more lives of our men and women in uniform by the development of lightweight protective armors for the soldiers. The value of nanotechnology to DOD includes, but is not limited to, the following:

a) *Chemical and biological warfare defense*. Nanotechnology will lead to the development of biochemical sensors to monitor the environment in the battlefield. Chemical and biological warfare agents must be detected at very low levels in real time. Nanotechnology will dramatically improve detection sensitivity and selectivity, even to the point of responding to a few molecules of the biochemical agent. Nanostructures are showing the potential for decontamination and neutralization as well.

b) *Protective armor for the warrior*. Nanotechnology will lead to the development of extremely strong and lightweight materials to be used as bullet-stopping armors.

c) *Reduction in weight of warfighting equipment*. Nanotechnology will reduce the volume and weight of the warfighting equipment a soldier/marine must carry in the battlefield by further miniaturization of the sensor/information systems. Development in nanoelectronics and portable power sources based on nanotechnology will provide much-needed capability in information dominance in sensing, communication, situational awareness, decision support, and targeting.

d) *High-performance platforms and weapons*. By providing small structures with special properties that can be embedded into larger structures, nanotechnology will lead to warfighting platforms of greater-stealth, higher-strength, and lighter-weight structural materials. In addition to higher performance, new materials manufactured by nanotechnology will provide higher reliability and lower life-cycle cost. One example, already in fleet test by the Navy, utilizes nanostructured coatings to dramatically reduce friction and wear. In another example, nanocomposites where clay nanoparticles are embedded in polymer matrices have been shown to have greater fire resistance and can be used onboard ships.

e) *High-performance information technology (IT).* Nanotechnology is expected to improve the performance of DOD IT systems by several orders of magnitude. Current electronics devices will reach a limit at 100 nm size in another 5 years. Continued advances in IT will require further advances in nanotechnology. Information dominance in network centric warfare and the digital battlefield is critical to DOD in winning the wars of the future.

f) *Energy and energetic materials*. The DOD has a unique requirement for energetic materials. Fast-release explosives and slow-release propellants must have high energy density while retaining stability. Nanoparticles and nano-energetic materials have shown greater power density than conventional explosives. Nanopowdered materials have also shown promise for improved efficiency in converting stored chemical energy into electricity for use in batteries and fuel cells.

g) *Uninhabited vehicles and miniature satellites*. Nanotechnology will lead to further miniaturization of the technology that goes into uninhabited vehicles and miniature satellites. The Uninhabited Air Vehicles (UAVs) will have greater range and endurance due to the lighter payload and smaller size. Uninhabited Combat Air Vehicles (UCAVs), will have greater aerial combat capabilities without the g-force limitations imposed on the pilot. Uninhabited Underwater Vehicles (UUVs) will be faster and more powerful due to miniaturization of the navigation and guidance electronics.

DOD Programs

Because of the large potential for payoffs in enhancing warfighting capabilities, nanotechnology continues to be one of the top priority research programs within the Department of Defense. In the Office of the Secretary of Defense, the DURINT (Defense University Research Initiative on Nanotechnology) will continue to be funded out of the University Research Initiative (URI) program. All three services and DARPA have substantial investments in nanotechnology 6.1 basic research. New 6.2 applied research programs are being planned to transition the research results to develop the nanotechnology for DOD.

Advanced Military Education and Training

James Murday, Naval Research Laboratory

The U.S. military annually inducts 200 thousand new people, 8 percent of its person power. Further, the anticipated personnel attrition during warfare requires extensive cross-training. With public pressure to reduce casualties, there is increasing utilization of high technology by the military. Warfighters must be trained in its use, recognizing that the education level of the average warfighter is high school. These circumstances present the military with an education and training challenge that is exacerbated by the fact that personnel are frequently in remote locations — onboard ship or at overseas bases — remote from traditional education resources. The entirety of K-12 education in the United States has similar problems, so any program that successfully addresses military training needs will certainly provide tools to enhance K-12 education as well.

The convergence of nano-, bio-, info- and cognitive technologies will enable the development of a highly effective teacher's aide — an inexpensive (~$100) virtual learning center that customizes its learning modes (audio, visual, and tactile) to individuals and immerses them into a custom environment best suited for their rapid acquisition of knowledge.

Role of Converging Technologies

Nano. Nanotechnology holds the promise for relatively inexpensive, high-performance teaching aides. One can envision a virtual-reality teaching environment that is tailored to the individual's learning modes, utilizes contexts stimulating to that individual, and reduces any embarrassment over mistakes. The information exchange with the computer can be fully interactive — speech, vision, and motion. Nanodevices will be essential to store the variety of necessary information or imagery and to process that information in the millisecond timeframes necessary for realtime interaction.

Bio. Biotechnology will be important to provide feedback on the individual's state of acuity and retention.

Info. Information technology must develop the software to enable far more rapid information processing and display. Since military training must include teaming relationships, the software must ultimately accommodate interaction between multiple parties. Innovations are also needed to enable augmented-reality manuals whereby an individual might have realtime heads-up display of information that cues repair and maintenance actions.

Cogno. Effective learning must start with an understanding of the cognitive process. People have different learning modes — oral, visual, tactile. They respond to different motivators — individual versus group — and different contexts — sports for the male, social for the female, to use two stereotypes. Human memory and decision processes depend on biochemical processes; better understanding of those processes may lead to heightened states of acuity and retention.

Transforming Strategy to Reach the Vision

Under its Training and Doctrine Command (TRADOC, http://www-tradoc.army.mil/), the U.S. Army has a Training Directorate that endeavors to introduce more effective training and education methods. A collaborative program between the National Nanotechnology Initiative, the National Information Technology Initiative, NSF (science and math), the Department of Education (K-12 teaching), and TRADOC might lead to the most rapid progress toward this goal. The entertainment industry must also be included, since it has been a driver behind much of the recent technological progress

Estimated Implications

This opportunity has benefit for education and training of students at all age levels, not just the military. Further, all technology benefits from larger markets to lower the unit cost. A low-cost instruction aide as described above, especially in mathematics and science, could bypass the problem of preparing adequately knowledgeable K-12 teachers. Success at this project could revolutionize the nation's approach to education.

VISIONARY PROJECTS

HIGH-PERFORMANCE WARFIGHTER

James Murday, Naval Research Laboratory

If one were to set out to find situations where the confluence of nano, bio, info and cogno technologies would make a critical difference, the military warfighter would certainly be seriously considered as a leading example. The warfighter is subjected to periods of intense stress where life or death decisions (cogno) must be made with incomplete information (info) available, where the physiology of fatigue and pain cloud reason (bio), and where supplemental technology (nano) must compete with the 120 pounds of equipment weight s/he must carry.

The confluence of the NBIC technologies will provide the future U.S. warfighter with the capability to dramatically out-fight any adversary, thereby imposing inhibitions to using warfare with the United States as a means to exert power and reducing the risk of U.S. casualties if warfare does occur.

Role of Converging Technologies

Nanotechnology holds the promise to provide much greater information, connectivity, and risk reduction to the warfighter. The continued miniaturization of electronic devices will provide 100 times more memory (a terabit of information in a cm^2). Processing speeds will increase to terahertz rates. Displays will be flexible and paper thin, if not replaced by direct write of information on the retina. High-bandwidth communication will be netted. Prolific unattended sensors and uninhabited, automated surveillance vehicles under personal control will provide high data streams on local situations. The marriage of semiconductors and biology will provide physiological monitors for alertness, chemical/biological agent threat, and casualty assessment. Nanofibers and nanoporous adsorbents will protect against CB threats while minimizing heat burdens and providing chameleon-like color adaptation for camouflage. The small size of the nanodevices will limit the volume, weight, and power burdens.

Presuming nanotechnology delivers the hardware, advances must be made to create information out of the manifold data streams. The soldier must stay alert to the environment, heads-up or retinal displays are essential, as well as the traditional flat, flexible (paper-like) media. Voice dialogue with the computer is essential to keep hands free for other functions. GPS-derived location, high-precision local maps (cm^2 voxels — potentially three-dimensional representations that include information about building structures, underground tunnels, and the like); language translators (for interrogation of the local citizenry); automated weapons that track target location and control the precise moment to fire: all of these capabilities will require new software.

Biotechnology promises considerable advances in monitoring and controlling the physiological condition of a warfighter. New innovations are likely to include sensitive, selective transduction of biological events into signals compatible with electronic devices; new approaches to the neutralization of biological and chemical agents without aggressively attacking other constituents in the local environment; and possible harnessing of body chemistry as a source of local power.

The nano-, info-, biotechnology items above are aides toward more effective learning and decision making. Rapid, effective cognition is critically dependent on body physiology, and on the manner information is organized and delivered (audio, visual, tactile) (Figure E.13).

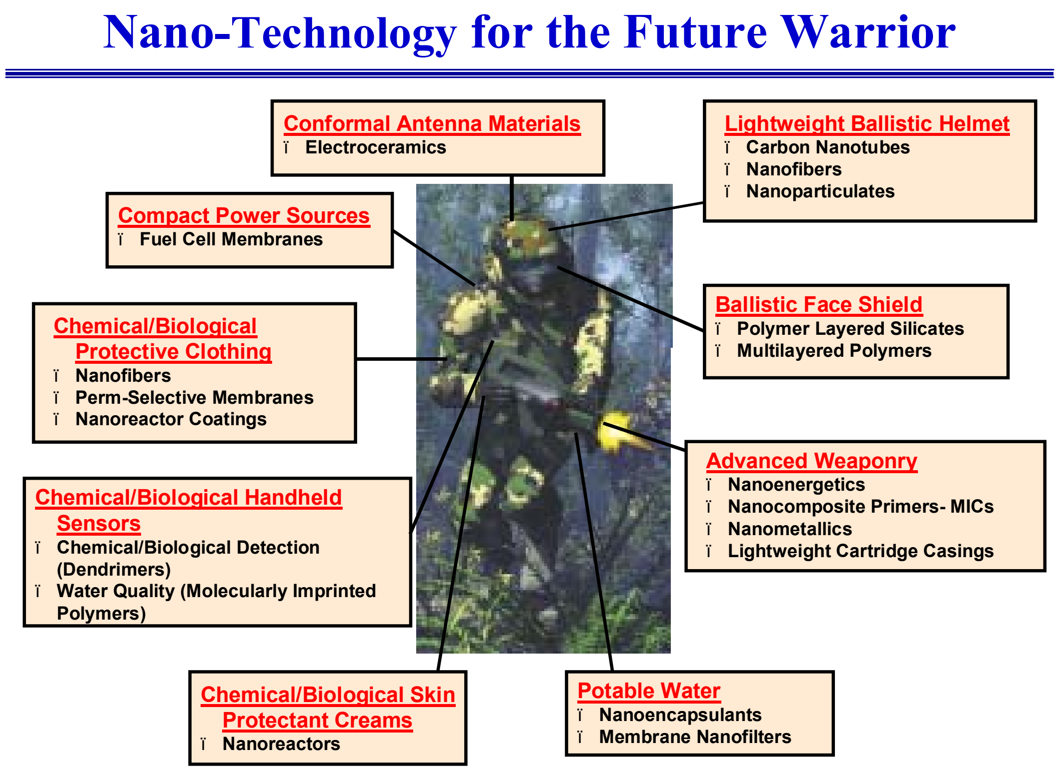

Figure E.13. Soldier system of the future (courtesy Dr. Andrzej W. Miziolek, U.S. Army Research Laboratory, AMSRL-WM-BD, Aberdeen Proving Ground, MD).

Transforming Strategy to Reach the Vision

Nanoscale science, engineering, and technology will provide the understanding critical to rapid progress in the development of new, higher-performance, information technology nanodevices, of high performance materials, and of sensors/activators for biological systems. In a simplified, but useful, perspective, nanoscience will underpin the information technology and biotechnology components of a warfighter system program. The National Nanotechnology Initiative (NNI) will provide a broad-based program in nanoscience; it remains a challenge to couple that program most effectively with information technology and biotechnology.

Information Technology (ITI) is also a U.S. national initiative. The coordinating offices for both the NNI and ITI programs have been collocated in order to encourage close collaboration. The Information Technology Initiative identifies areas where advances in device capability would be most effective and works to advance modeling and simulation (high-performance computing) so that theoretical contributions to nanoscience will be an equal partner with the experimental efforts. The Nanotechnology Initiative must accelerate progress in those areas where new, cost-effective technology will lead to the most significant impact on information systems.

Biotechnology is effectively a third U.S. national imitative if one includes the NIH budget for health and medicine. A principal challenge here is acceleration of chemical, physical, materials, and engineering contributions to biotechnology. Biology must also better identify the biochemical basis for alertness, acuity, and memory retention.

The large investments already present in nano-, info- and biotechnology should be coordinated and coupled with efforts in cognition. DARPA, NASA, NIH, and NSF already have major programs that seek to integrate nano-, bio- and info- research. Within the DOD, the Army and Marines have the lead efforts in technologies to impact the individual warfighter. The Army is presently competing a University-Affiliated Research Center (UARC) on the topic, "Institute for Soldier Nanotechnologies," that potentially can integrate the essential components of this opportunity.

Estimated Implications

Technology has led to dramatic improvements in fighting capability, but not for the individual soldier or marine. While air and sea power certainly have a major role in attacking any opponent, in any major conflict, soldiers and marines will be engaged in ground combat. Utilizing the convergent NBIC technologies, we have the opportunity to improve significantly the ability to control the local situation at minimal risk of personal casualty.

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NON-DRUG TREATMENTS FOR ENHANCEMENT OF HUMAN PERFORMANCE

Robert Asher, Sandia National Laboratories

Human performance enhancement may require modifications to the biochemical aspects of the human. Maintained alertness, enhanced physical and psychological performance, and enhanced survivability rates in serious operations all require modifications to the biochemical aspect of the human. DARPA is in the process of developing drugs to enhance performance when a person has been sleep-deprived. Drug companies spend an average of $800 million to develop new drugs that may have negative side effects. An alternative is to develop non-drug approaches to human performance enhancement. As an example, it is common medical practice to immerse a person in a hot bath preceding heart operations to build up stress proteins that will give greater survivability when s/he receives blood products.

Figure E.14. Wearable device for non-drug treatments.

Consider the use of externally applied, non-dangerous electromagnetic fields to increase the rate of production of body biochemicals that enhance human performance. DARPA has a proposal to increase the rate of stress protein production before a soldier goes into combat. The intent is to increase the survivability rate when the soldier is wounded and needs to receive blood products. Beyond that, one can envision increasing the rate of production of ATP, which will yield higher energy levels by natural means, will help ion pumping to aid in nerve recovery and contraction of muscles, and will speed recovery from combat stress. What other changes can be engineered by a specifically shaped electromagnetic pulse that might enhance human performance without pharmaceuticals? This investigation may spawn a new industry in which the human is enhanced by externally applied electromagnetic pulses so shaped so as to enhance specific biochemical changes within the body without drugs or in combination with drugs, with fewer side effects. For instance, nanoparticles might be formulated to release drug dosages only when irradiated with electromagnetic pulses focused at certain sites, allowing treatments to specific areas without the whole body being affected by the drug therapy.

Role of Converging Technologies

All of the NBIC technologies have a role in the goals of non-drug enhancement of human performance:

Nano. Develop and understand the nano aspects of the use of electromagnetic field interactions with cellular structures. Develop and understand how treatments may be developed by nano particle interactions only at specific sites where the electromagnetic fields are focused. Investigate whether electromagnetics can be used as a power source to conduct mechanical actions at the sites.

Bio. Develop a detailed understanding of the effects of electromagnetics on cells and neuronal networks, including the full range of scales, from micro effects on proteins to macro effects on neuronal networks.

Info. Develop methods to shape optimal electromagnetic pulses to carry messages to the cells and neurons.

Cogno. Understand how electromagnetics can be used to enhance cognitive performance as well as physiological performance.

Transforming Strategy to Reach Vision

The strategies to achieve these goals are as follows:

- Develop a program that will explore the use of electromagnetics for enhancement of human performance. This program will be multidisciplinary in orientation, utilizing
  - electromagnetics as the actuation mechanism for the treatments
  - biotechnology in the understanding of cellular interaction with the electromagnetic fields
  - nanotechnology to help engineer solutions that may include specific site treatments released by a focused electromagnetic field
  - information technology in that the pulses need to be so shaped as to cause desired interconnected cell electromagnetic responses of cognition by external fields
- Fund work towards the goal of understanding in detail the effects of electromagnetics on cellular systems and on cognition.
- Consider cellular electrochemical and structural changes and actions imposed by electromagnetics.

- Fund work towards electromagnetic and biochemical dynamical modeling of cellular systems in order to both understand electromagnetic and biochemical aspects, as well as to optimize the shape of electromagnetic pulses to impose desired cell changes without inducing side effects.
- Fund experimental basic work in understanding the effects of electromagnetics on cells.

Estimated Implications

The impact on society of such a program can be great, as this might yield treatments to enhance human performance without the use of drugs and provide new exciting treatments for ailments that require site-specific treatments. A new industry can be born from this work. It may also lead to treatments that will enhance human cognition.

BRAIN-MACHINE INTERFACE

Robert Asher, Sandia National Laboratories

Increasingly, the human is being asked to take in multisensory inputs, to make near-instantaneous decisions on these inputs, and to apply control forces to multitask and control machines of various sorts. The multitasking, multisensor environment stresses the human, yet, more and more s/he being asked to operate in such an environment. As an example, the visionary project on uninhabited combat vehicles discusses an increased workload in piloting combat vehicles. DARPA has a brain-machine interface program about to start. This program has as its goal human ability to control complex entities by sending control actions without the delay for muscle activation. The major application for this program is control of aircraft. The intent is to take brain signals and use them in a control strategy and then to impart feedback signals back into the brain.

The DARPA program could be extended to include a broader range of potential impact by including the possibility of other applications: learning and training, automobile control, air traffic control, decision-making, remote sensing of stress, and entertainment. Learning and training might be implemented as information coded into brain signals and then input into the person. Air traffic control in increasingly busy skies can use such capability: the controller has multiple inputs from multiple aircraft. These can be input into his brain in a 3-D aspect and an alertness signal used to “wake him up” when his attention drifts beyond acceptable limits. Not only intellectual data might be passed from one person to another without speaking, but also emotional and volitional information. Decision-making may become more precise as emotional, fatigue, and other cognitive states can be appraised prior to making a critical decision.

The potential impact on automobile safety is great. The driver can have quicker control of his automobile (Fig. E.15), allowing for safer driving while reducing the car-to-car spacing on congested highways. This would help alleviate highway congestion and the need for more highways. Furthermore, it would allow for safer driving as driver attention can be measured and the driver “alerted” or told in some manner to pay attention to his or her driving when attention wanders beyond safe margins. It can allow for detection of driver impairment so that the vehicle may be made either not to start or to call emergency.

Direct connection into the brain could yield a revolution in entertainment, as people may be “immersed,” MATRIX-style, into the midst of a movie or educational show. Can you imagine the impact of being immersed in a fully 3-D audio-visual simulation of the battle of Gettysburg?

Figure E.15. Hands-off control of an automobile through a device for reading and implanting brain waves.

Role of Converging Technologies

Nano. The brain-machine interface effort will require nanotechnologies in order to make the required experimental measurements and to implement the devices for both receiving brain electromagnetic signals and transmitting signals back into the brain.

Bio. This is a highly biological, neuroscience effort, which requires detailed understanding and measurements of the brain's electromagnetic activity. It requires a significant measurement protocol.

Cogno. This effort by its very nature will directly affect the cognitive aspects of the individual by externally applied electromagnetic fields by implanting information for the individual. Thus, this effort can lead to increased learning and other cognitive results.

Transforming Strategy to Reach the Vision

To achieve these goals, enter a partnership with DARPA to fund additional technologies and applications that would enhance the brain-machine interface effort. Work should be focused on the goals of using the technologies for cognitional aspects, understanding memory, and learning brain function to be able to design devices to increase their capabilities.

Estimated Implications

This effort would yield a technological revolution, in applications from computers to entertainment. It would give the United States a global competitive advantage while yielding solutions to specific domestic problems such as air traffic control and highway safety in increasingly crowded environments. It will revolutionize education. This effort will yield devices that may be applied to a number of activities and be sufficiently small as to be wearable in a car or at home.

NANO-BIO-INFO-COGNO AS ENABLING TECHNOLOGY FOR UNINHABITED COMBAT VEHICLES

Clifford Lau, Office of the Deputy Under Secretary of Defense for Research

It is envisioned that in 20-30 years, when the research and development are successfully completed, nano-bio-info-cogno (NBIC) technology will enable us to replace the fighter pilot, either autonomously or with the pilot-in-the-loop, in many dangerous warfighting missions. The uninhabited air vehicle will have an artificial "brain" that can emulate a skillful fighter pilot in the performance of its missions. Tasks such as take-off, navigation, situation awareness, target identification, and safe return landing will be done autonomously, with the possible exception of person-in-the-loop for strategic and firing decisions. Removing the pilot will result in a more combat-agile aircraft with less weight and no g-force constraints, as well as reduce the risk of pilot injury or death. The fighter airplane will likely derive the greatest operational advantages, but similar benefits will accrue to uninhabited tanks, submarines, and other military platforms.

Role of Converging Technologies

The convergent NBIC technologies, although at the early stage of basic research, are anticipated to have an impact on practically all arenas of warfighting and peacekeeping and thus are vitally important to national security. For instance, today's fighter airplanes are loaded with sensors, avionics, and weapon systems. The complexity of these systems and the information they provide place tremendous workload on the pilot. The pilot must fly the fighter airplane in hostile environment, watch the cockpit displays, be aware of the situation, process the sensor information, avoid anti-air missiles, identify and destroy the targets, and return safely. There is no wonder there is information overload on the pilot, in spite of the many decision aid systems. Furthermore, fighter pilots are highly valued and trained warriors, and the country cannot afford to lose them from anti-air fire. The need for autonomous or semi-autonomous air vehicles to accomplish surveillance and strike missions is clear (Fig. E.16).

Nano. Nanotechnology will continue to the current trend in miniaturization of sensors, electronics, information processors, and computers. Miniaturization will reduce the weight, size, and power of the on-board systems in the air vehicle, and will increase information processing power.

Bio. Brain research will help us to understand how pilots process the massive amount of information coming from the sensors and intelligence. That understanding will allow us to design an artificial "brain" to process the information and to control the air vehicle autonomously.

Info. Research in information technology will enable us to design specialized systems that do not require the writing of millions of lines of code, such as the adaptive learning strategy used by the brain. Storage and retrieval of massive amounts of data and information fusion to allow the system to make decisions will also be an important aspect of this research.

Cogno. Understanding the principles behind cognition is extremely important in the design of an autonomous system with the capabilities of target recognition and situation awareness. For autonomous air vehicles, it is particularly important to recognize the intent of encounters with friendly or unfriendly aircraft in its vicinity.

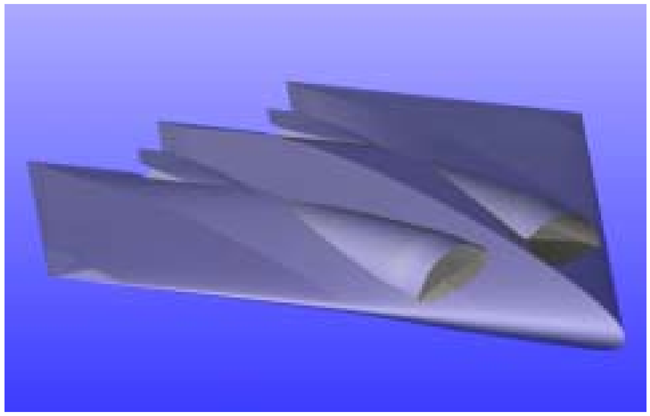

Figure E.16. Uninhabited Combat Air Vehicle (UCAV).

Transforming Strategy to Reach Vision

The DOD presently has a number of projects working toward uninhabited combat aircraft. The challenges to meet this goal are considerable. An NBIC program centered at universities would provide both the scientific discovery and the trained students that will be necessary for those projects to succeed quickly. In order to achieve the vision stated above, it is necessary to plan a coordinated and long-term research program considering the above strategies on how to get there. It is important to integrate the current research efforts on nanotechnology with the other research areas to form a multidisciplinary research program. A university-based basic research program addressing the needed science must be interactive with the DOD programs addressing system design and manufacture.

Estimated Implications

Removal of the pilot from assault and fighter aircraft will reduce the risk of injury or death to highly trained warfighters. American public opinion makes this a clear priority. In addition, the lighter weight (no pilot, oxygen system, ejection system, man-rated armor, canopy, etc.) and absence of human g-force constraints will make the aircraft either more maneuverable or capable of more extended missions.

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DATA LINKAGE AND THREAT ANTICIPATION TOOLS

Tony Fainberg, Defense Threat Reduction Agency

The United States will be subject to asymmetric military threats from lesser powers. On 11 September 2001, this observation moved from the theoretical to the real. To deal adequately with the future, the United States must develop an intelligence system to anticipate threats from adversary states or sub-state actors.

Role of Converging Technologies

The suggested approach is to use the power of *information technology* to assemble, filter, and analyze data about the adversary. First, it will be necessary to acquire a large volume of data regarding each potential enemy organization. Data linkage among many databases would be needed, including some from open source material and others from intelligence sources. The data would include the group's characteristics, its people, funds, and the movement of each, the motivations of the people, relevant current events, significant dates, and some way of encoding the cultural perspectives of the organization. In addition to information technology, the approach also requires *nanotechnology*, due to the large amount of data that need to be handled and analyzed. Further, some sociological analysis (for the group) and psychological profiling would be required, as well as country and culture experts. This requires broad social science input. Understanding how the adversary analyzes and makes decisions involves modeling his *cognition* processes. An automated translation capability would be helpful in the data mining, since frequently there may not be enough analysts familiar with the necessary languages to keep up with the data input.

Transforming Strategy to Reach Vision

DARPA's Information Technology Office is pursuing similar methodologies, as have, no doubt, other branches of the government. It is possible that increased computing power, better application of the social sciences, plus more sophisticated integration of the information and modern decision algorithms might produce significantly better predictive tools. The National Science Foundation is in an excellent position to sponsor research in this area, as well as to coordinate similar programs of other agencies through interagency workshops.

Estimated Implications

The resulting decision tool or decision aid would probably not be able to predict a specific event at a specific time; however, it could possibly function to cue intelligence services to look more closely at the adversary when it gives an alarm and might also be useful for cueing heightened security alerts.

F. UNIFYING SCIENCE AND EDUCATION

THEME F SUMMARY

Panel: D.L. Akins, Y. Bar-Yam, J.G. Batterson, A.H. Cohen, M.E. Gorman, M. Heller, J. Klein-Seetharaman, A.T. Pope, M.C. Roco, R. Reddy, W. Tolles, R.S. Williams, D. Zolandz

The fifth and final NBIC theme explores the transformations of science and scientific education that will enable and be enhanced by technological convergence. The panel especially focused on the ways that education can transform science and unifying science (based on the unity of nature and using cause-and-effect explanation) can transform education, for the vast improvement of both. As a number of reports from the National Research Council (NRC 1996-2000) and comparable organizations attest, the future of society depends on continued scientific progress, which in turn depends upon science education. Converging scientific principles and technologies will raise the importance of this issue to a higher level.

Four factors demand significant changes in the science education received by students at all levels:

i) Many poorly understood social factors work against science in the educational system, and ways must be found to counter these anti-science forces using new S&T trends (NSF 2000).

ii) Rapid progress in cognitive, biological, information, and nanoscale sciences *9offers new insights about how people learn that can guide effective reforms in curriculum, evaluation, and organizational structuring.

iii) New education techniques and tools will be made available by converging technologies, and we need to prepare to take advantage of them.

iv) Few mid-career professional scientists have the practical opportunity to redirect their careers to any significant extent, so unification of the sciences must largely begin in school.

Currently, scientific and engineering education is highly fragmentary, each part constrained by the boundaries of one particular discipline. In the future, the knowledge taught will be based on unifying concepts offered by nano, bio, info, and cognitive sciences throughout the educational establishment. Natural, engineering, social, and humanity sciences will converge. The corresponding basic concepts of unifying science will be introduced at the beginning of the teaching process in K-12, undergraduate, and graduate education. New tools will be developed by convergent technologies to provide high-quality, anywhere-anytime educational opportunities. NBIC science and engineering education will be made available to the majority of students and as continuing education to all interested adults.

No single discipline can describe or support the converging technologies by itself. Different disciplines may play a leading role in different applications. Interfaces are beginning to develop among the four NBIC domains, linking them in pairs, trios, and as a full quartet, in parallel with in-depth development within each field. The optimal process will not develop naturally: a systematic program must be created to encourage it.

Within academia, significant challenges must be overcome. Many teachers lack sufficient depth in their knowledge of mathematics and science, and not enough of the best students are attracted to science and technology. Also, qualified personnel who do understand science and technology generally get better-paying jobs outside the field of teaching.

What Can NBIC Do for Education?

The unification of the sciences is gaining momentum and will provide a knowledge base for education. The concepts on fundamental building blocks of matter employed in nanoscience can be applied in different disciplines, thus providing a multidisciplinary opportunity to introduce breadth while advancing depth. This creates the opportunity for integration across learning — moving from reductionism to integration. It also introduces the challenge of creating a common language for talking about the big picture.

Technologies that arise from the NBIC convergence will provide new tools and modalities for teaching. Some of these will be sensory, including visual, auditory, and tactile. Others will take advantage of better understanding of how the brain works. Still others will be logistic and include delivery of teaching and educational resources anytime and anywhere. For advanced levels of scientific training, this will create opportunities at new research frontiers.

Across all levels, there will be opportunities to involve groups of people who have tended previously to be excluded from high-quality science education. We have a responsibility to achieve substantial inclusion and outreach, especially across race and gender. The entire 21st century workforce will be involved in the convergent technologies revolution. NBIC-related applications will be an excellent way to promote systemic, problem-based learning from the earliest educational levels.

What Can Education Do for NBIC?

Universities epitomize the ideal of uniting the intellectual heritage of mankind, so they are a relatively hospitable environment for scientific and technological convergence. Other kinds of educational institutions can also play crucial roles in bringing the scientific and technical disciplines together. In the economy, certain markets become trading zones where a great diversity of products, services, and institutions converge. Scientific trading zones will have to be created, perhaps anchored in university-based research centers or in joint academic-industrial partnerships, that will allow students and scientists to develop the necessary communication skills for trading ideas across disciplines.

The educational system can provide a stimulus for drawing recruits into the NBIC community. Classrooms can become a proving ground for exploring new technologies designed to facilitate learning and communication. Similarly, the educational system can be a developmental laboratory for testing useful technological directions in NBIC.

Many new educational approaches will have to be tried in order to see which are most effective in achieving technological convergence. For example, universities may offer retraining for scientists who already have doctorates and may already have extensive experience in industry or research laboratories. Perhaps young scientists will engage in post-doctoral work in a second field. NBIC will benefit from changes in life-long learning at all levels, including in both white-collar and blue-collar occupations. NBIC concepts must be adopted early, in advance of technological developments that would require a qualified workforce.

NBIC is likely to be both creative and destructive at all levels of the scientific, economic, and social establishment, for example, creating new industries and companies, with the inescapable result that some older ones will decline or even become extinct. Thus, it will be important to educate society about the potential unintended consequences of technological innovation. Maximizing the societal benefits of a new technology is essential for it to enjoy full public support (Roco and Bainbridge 2001).

NBIC Education for the Twenty-First Century

To enhance human performance most successfully, science and engineering education will have to evolve and, in some respects, radically reinvent itself. The knowledge taught will be based on concepts offered by nano, bio, info, and cognitive sciences, and these concepts will be introduced at the beginning of the K-12 teaching process. High-quality science education will be made available to the majority of students.

Special efforts must be made to stimulate communication between disciplines and develop in scientists the communication skills for doing so, so that conversations between them can be made focused and productive. Achievement of good interdisciplinary communication will synergistically enhance the knowledge and progress of all disciplines. Since mathematical tools represent a common language among and between disciplines, mathematics should be taught in greater depth and be a common focus among most scientific disciplines. At the same time, mathematics textbooks must use problems from science and engineering as examples.

Concerted efforts must be supported to write cross-disciplinary educational materials, using a variety of media at the university level that help with the language problems across traditional fields. A positive, inclusive social environment must be promoted that encourages creative growth of converging technologies. Improved pedagogy and accessibility are fundamental ingredients for the realization of converging technologies, incorporating the cultural differences that exist between students and between different technical fields.

At the college and graduate school levels, we may need a new program for multidisciplinary fellowships that would make it possible for students to move among professors and disciplines related to NBIC. A fellowship might travel with a student from one department or school to another and temporarily into a research integration or industry unit. Students might be allowed to define their own cross-disciplinary proposals, then funding would be provided directly to them rather than to an institution or mentor.

Depth in graduate studies is necessary and should not be compromised. However, if specific disciplines deliberately associate themselves with neighboring disciplines that use similar tools and models, breadth and a holistic perspective will come more easily to all.

Creating new educational curricula and methodologies will require problem-driven, system-oriented research and development. Cognitive scientists can analyze learning styles using NBIC and provide appropriate assistance. Better education is needed for teachers, including sufficiently funded research experiences and credit for in-service experiences in industry and research laboratories.

NBIC concepts should be introduced as early as possible. For example, basic concepts and problems of nanoscience could be taught in elementary schools. NBIC terms and concepts could be placed into childhood educational reading materials starting from the earliest levels. Virtual reality environments and websites could offer many kinds of exciting instructional materials. Practical demonstration kits could facilitate interactive learning. Research scientists could frequently visit schools to offer demonstrations and serve as role models.

NBIC courses and modules can be integrated to some extent into existing curricula and school settings, but novel alternatives will also have to be explored. Every way of making science and technology more interesting for young people would be helpful, such as using games to teach math and logic. To achieve these goals, it will be essential for educators, including members of school boards, curriculum development committees, and designers of standardized tests, to identify and encourage champions in K-12 schools. National standards for educational achievement will be indispensable tools to address the most challenging and promising NBIC areas.

In fifteen years, we anticipate that education will be based to a significant extent on unifying principles in science and technology that are easier to understand and more valuable for the learner. The new NBIC science content will have been introduced and be available in about 50 percent of the public schools. A variety of new pedagogical tools will be widely available, based on new learning methods, using learning-enhancing devices developed by neuroscience in cooperation with information technology. The process of learning at home or school, either individually or in groups, will be faster and better because of the new methods, tools, and processes.

Statements and Visions

As in the other working groups, participants in the Science and Education group prepared statements offering strategies for transforming the current situation with respect to scientific unification and visions of what could be accomplished in ten or twenty years. Several contributors examined the social and intellectual processes by which sciences and technologies converge (M. Gorman, J. Batterson and A. Pope, and Y. Bar-Yam); others focused on the special education opportunities offered by integrating sciences from the nanoscale (W. Tolles and A. Cohen); on fully involving human resources (D. Akins); and on enhancing human abilities using biological language (J. Klein-Seetharaman and R. Reddy).

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STATEMENTS

COMBINING THE SOCIAL AND THE NANOTECHNOLOGY: A MODEL FOR CONVERGING TECHNOLOGIES

Michael E. Gorman, University of Virginia

The National Science Foundation (NSF) is considering societal implications as the new field of nanotechnology emerges, rather than wait for major problems to occur before attempting a fix. This concern for ethics at the earliest stages of discovery and invention needs to be extended to converging technologies as well, a theme to which I will return. But at the outset, I will limit my remarks to nanotechnology, following up on the 2001 NSF meeting on this topic (Roco and Bainbridge 2001).

H. Glimell (2001) has discussed how new fields like nanotechnology create the need for work at the boundaries between fields:

> Consider for example molecular electronics compared with bio-nano (or the interface of biological and organic nano materials). The actors, nodes and connections to appear in the extension of these NSE subareas obviously constitute two very different networks of innovation. Nanoelectronics is being negotiated and molded in between two camps — the conservative mainstream of the microelectronics industry with its skepticism towards anything popping up as a challenger to the three decade old CMOS technology trajectory, and the camp committed to a scenario where that trajectory might come to its end within some five years from now. (Glimell 2001, 199)

Peter Galison (1997) uses the metaphor of a trading zone between different cultures to describe cooperative work at boundaries. One of his examples is the collaboration between physicists and engineers in the Radiation Laboratory at MIT during World War II: "Each of the different subcultures was forced to set aside its longer term and more general symbolic and practical modes of work in order to construct the hybrid of practices that all recognized as "radar philosophy." Under the gun, the various subcultures coordinated their actions and representations in ways that had seemed impossible in peacetime; thrown together they began to get on with the job of building radar" (Galison 1997, 827). Despite differences in training and expertise, engineers and physicists of varying backgrounds were able to trade important information.

The current debates about nanotechnology are signs of an expanded trading zone. As Etkowitz has pointed out (2001), the physical sciences need to find a way to emulate the success of the life sciences while avoiding the ethical and social problems that have emerged as genetically modified organisms hit the market. Hence, several extravagant promises have been made about nanotechnology, promises that lead to concerns about what would happen if these promises were fulfilled — if, for example, self-replicating nanobots were ever created. The hardest thing to predict about a new technology is the interaction effect it will have with other evolving social and technical systems.

Thomas Park Hughes, a historian of technology who has spent a lifetime studying the invention of large technological systems, discusses how reverse salients attract inventors: "A salient is a protrusion in a geometric figure, a line of battle, or an expanding weather front. As technological systems expand, reverse salients develop. Reverse salients are components in the system that have fallen behind or are out of phase with the others" (Hughes 1987, 73). In the 1870s, progress in telegraphy was hindered by the fact that only two messages could be sent down a single wire at the same time: the classic problem of bandwidth.

What are the reverse salients that attract researchers and funding to nanotechnology? One is Moore's Law, which reaches asymptote very quickly unless a way can be found to shrink integrated circuits to the nanoscale. This current reverse salient is an instance of a historical one. Earlier, it was vacuum tubes that held up progress in computing. Transistors solved that problem, but then formed their own reverse salient as computing needs expanded to the point where "Production of the first 'second generation' (i.e., completely transistorized) computer — the control data CD 1604, containing 25,000 transistors, 100,000 diodes, and hundreds of thousands of resistors and capacitors — lagged hopelessly behind schedule because of the sheer difficulty of connecting the parts" (Reid 1984, 18). The apparent solution was miniaturization, but there were physical limits. The solution was to transform the problem: instead of building tiny transistors, create an integrated circuit. Nanotechnology offers a similar way of transcending the limits of microchip technology.

Another reverse salient is mentioned by several of contributors to the 2001 Report on the Societal Implications of Nanoscience and Nanotechnology of the Nanoscale Science, Engineering, and Technology (NSET) of the National Science and Technology Council (Roco and Bainbridge 2001). This is the ability to study and emulate fine-grained cellular structures. "Follow the analogy of nature" is a common invention heuristic that depends on an intimate knowledge of nature. Bell used this heuristic to transform the telegraph reverse salient in the 1870s. Instead of an improved device to send multiple messages down a single wire, he created a device to transmit and receive speech, using the human ear as a mental model. Bell's telephone patent formed the basis for one of the great communications start-ups of all time, the Bell Telephone Corporation, which surpassed Western Union, the Microsoft of its day (Carlson 1994). Similarly, detailed understanding of cellular processes at the nanoscale will lead to new devices and technologies that may transform existing reverse salients.

A potential set of reverse salients that came up repeatedly in the 2001 NSET report are environmental problems like ensuring clean water and providing adequate energy.

The terrorist attacks on September 11th will create a new series of reverse salients, as we think about ways of using technology to stop terrorism — and also of protecting against misuses of technology that could contribute to terrorism. Research should be directed towards determining which aspects of these broad reverse salients can be converted into problems whose solutions lie at the nanoscale. One important goal of such research should be separating hype from hope.

Role of Practical Ethics Combined with Social Science

The focus of practical ethics is on collaboration among practitioners to solve problems that have an ethical component. Similarly, social scientists who work in science-technology studies typically establish close links to practice. There are four roles for practical ethics linked to social sciences:

- Prevention of undesirable side effects
- Facilitation of quality research in nanotechnology by social scientists
- Targeting of converging technology areas of social concern
- Incorporation of ethics into science education

Prevention of Undesirable Side Effects

What are the potential negative impacts of nanotechnology, as far as important segments of society are concerned? How can these be prevented? The 2001 NSET report made frequent reference to the negative press received by genetically modified organisms (GMOs) as exactly the kind of problem nanotechnology practitioners wish to avoid. Monsanto, in particular, has developed a variety of genetically modified seeds that improve farmer yields while reducing use of pesticides and herbicides. But Monsanto did not include consumers in its trading zone, particularly in Europe, where potential customers want GMO products labeled so they can decide whether to buy. The best prevention is a broad trading zone that includes potential users as well as interested nongovernmental organizations like Greenpeace in a dialogue over the future of new nanotechnologies. Social scientists and practical ethicists can assist in creating and monitoring this dialogue.

A related area of concern is the division between the rich and poor, worldwide. If new nanotechnologies are developed that can improve the quality of life, how can they be shared across national boundaries and economic circumstances in ways that also protect intellectual property rights and ensure a sufficient return on investment? Consider, for example, the struggle to make expensive AIDS medications available in Africa. Again, proper dissemination of a new technology will require thinking about a broad trading zone from the beginning. Social scientists can help establish and monitor such a trading zone.

Nanotechnology offers potential national security benefits (Tolles 2001). It might be possible, for example, to greatly enhance the performance of Special Forces by using nano circuitry to provide each individual soldier with more information. However, there are limits to how much information a human being can process, especially in a highly stressful situation. This kind of information might have to be accompanied by intelligent agents to help interpret it, turning human beings into cyborgs (Haraway 1997). Kurzweil (1999) speculates that a computer will approximate human intelligence by about 2020. If so, our cyborg soldiers could be accompanied by machines capable of making their own decisions. It is very important that our capacity for moral decision-making keep pace with technology.

Therefore, practical ethicists and social scientists need to be involved in the development of these military technologies. For example, cognitive scientists can do research on how a cyborg system makes decisions about what constitutes a legitimate target under varying conditions, including amount of information, how the information is presented, processing time, and quality of the connection to higher levels of command. Practical ethicists can then work with cognitive scientists to determine where moral decisions, such as when to kill, should reside in this chain of command.

Military technology faces barriers to sharing that are much higher than intellectual property concerns. The cyborg soldier is much more likely to come from a highly developed country and face a more primitive foe. However, technological superiority does not guarantee victory — nor does it guarantee moral superiority. Practical ethicists and social scientists need to act as stand-ins for other global stakeholders in debates over the future of military nanotechnology.

Facilitation of Quality Research in Nanotechnology by Social Scientists

Improving the quality of research is one area of convergence between the nano and the cogno. Cognitive scientists can study expertise in emerging technological areas and can help expert nanotechnology practitioners monitor and improve their own problem-solving processes. Experts rely heavily on tacit knowledge, especially on the cutting-edge areas (Gorman n.d.). Portions of this knowledge can be shared across teams; other portions are distributed, with individuals becoming experts in particular functions. Cognitive scientists can help teams reflect on this division of labor in ways that facilitate collaboration and collective learning (Hutchins 1995). Cognitive methods can therefore be used to study and improve multidisciplinary convergence, including the development of new trading zones.

Targeting of Converging Technology Areas of Social Concern

Practical ethics and social sciences should not be limited to anticipating and preventing problems. Both can play an important role in facilitating the development of nanotechnology, by encouraging reflective practice (Schon 1987).

An important goal of this reflection is to eliminate the compartmentalization between the technical and the social that is so predominant in science and engineering (Gorman, Hertz et al. 2000). Most of the engineers and applied scientists I work with are solutions seeking problems. They are generally people of personal integrity who, however, do not see that ethics and social responsibility should be factors in their choice of problems. Technology can evolve without improving social conditions, but true technological progress requires social progress. Indeed, focusing on social benefits opens up a range of interesting new technological problems.

Practical ethicists can work with engineers and scientists to identify interesting and worthy social concerns to which the latest developments in nanotechnology could be applied. Philosophers and social scientists cannot simply dictate which problems practitioners should try to solve, because not all social problems will benefit from the application of nanotechnology, and not all future technologies are equally likely.

Directing a technology towards a social problem does not eliminate the possibility of undesirable side effects, and a technology designed to produce harm may have beneficial spin-offs. For example, Lave (2001) does an admirable job of discussing the possibility of unforeseen, undesirable effects when nanotechnology is applied to environmental sustainability. The probability of truly beneficial environmental impacts is increased by taking an earth systems perspective (Allenby 2001). Similar high-level systems perspectives are essential for other nanotechnology applications; in order to achieve this kind of perspective, scientists, engineers, ethicists and social scientists will have to collaborate.

Incorporation of Ethics into Science Education

How can practical ethicists and social scientists work with science and engineering educators to turn students into reflective nanotechnology researchers? I am Chair of a Division of Technology, Culture, and Communication at the University of Virginia, inside the Engineering School, which gives us a great opportunity to link social responsibility directly to engineering practice. We rely heavily on the case method to accomplish this (Gorman, Mehalik, et al. 2000). We also co-supervise every engineering student's senior thesis; we encourage students to think about the social impacts of their work. But we need to go a step further and encourage more students to pursue work linking the social, the ethical, and the technical.

This kind of linkage can attract students into engineering and science, especially if this sort of education is encouraged at the secondary level. Unfortunately, our secondary and elementary educational systems are now focused more on the kind of accountability that can be measured in examinations and less on the kind of creativity and perseverance that produces the best science and engineering. New educational initiatives in nanotechnology can play an important role in changing this climate.

A New Kind of Engineering Research Center

Several years ago, NSF sponsored an Engineering Research Center (ERC) that combined bioengineering and educational technology. Why not also sponsor an ERC that combines research and teaching on the societal implications of nanotechnology? Parts of this center could be distributed, but it should include one or more nanotechnology laboratories that are willing to take their fundamental science and apply it in directions identified as particularly beneficial by collaborating social scientists and practical ethicists. The goal would be "to infuse technological development with deeper, more thoughtful and wide-ranging discussions of the social purposes of nanotechnology…putting socially beneficial technologies at the top of the research list" (Nardi 2001, 318-19). Deliberations and results should be shared openly, creating an atmosphere of transparency (Weil 2001).

This center could combine graduate students in science and engineering with those trained in social sciences and ethics, thus forming a "living bridge" connecting experts from a variety of disciplines. Some graduate students could even receive training that combines engineering, ethics, and social sciences, as we do in a graduate program at the University of Virginia (Gorman, Hertz, et al. 2000).

The center should hold annual workshops bringing other ERCs and other kinds of research centers involved with nanotechnology together with applied ethicists and social scientists. There should be a strong educational outreach program designed to encourage students concerned with making the world a better place to consider careers in nanotechnology. Hopefully, the end-result would be a model for creating trading zones that encourage true technological progress.

This kind of a center need not be limited to nanotechnology. What about a science and technology center on the theme of converging nano, bio, info and cogno (NBIC) technologies directed towards maximum social benefit? One example of a potential NBIC product is of a smart agent able to look up the price and availability of a particular item and identify the store where it can be found while a consumer walks through the mall. This kind of technology has no benefits for the millions all over the world who are dying of AIDS, suffering from malnutrition, and/or being oppressed by dictators.

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BREADTH, DEPTH, AND ACADEMIC NANO-NICHES

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The report to the President titled *Science: The Endless Frontier* (Bush 1945) ushered in a period of rapid growth in research for 2-3 decades. This was stimulated further by the launch of Sputnik and programs to explore the moon. Over the past 56 years, research has moved from an environment where there was unquestioned acceptance of academic-style research by both academia and industry to an environment in which industry, in its effort to maintain profit margins in the face of global competition, has rejected the academic model of research and now focuses on short-term objectives. The need for industry to hire new blood and to generate new ideas is a major stimulus for cooperation between industry and academia. Academia has mixed reactions to these more recent trends. Universities are concerned about a loss of some independence and freedom to pursue new ideas in conjunction with industry, primarily due to the proprietary nature of maturing research/development. The pressures on academia to "demonstrate relevance" have continued for decades. In the search for "relevance," the concept of nanotechnology has emerged to satisfy a large community of researchers in both academia and industry.

The discovery of a new suite of experimental tools (beginning with scanning tunneling microscopy) with which to explore ever smaller features, to the level of the atom, reopened the doors joining the progress of academia to that of industry. The nanotechnology concept fulfilled the pressures of both the commercial world (pursuing continuation of the fruits of miniaturization) and academia (pursuing opportunities to research the many new pathways opened by these tools). The umbrella term "nanotechnology" covers programs already underway in both communities, thus giving a stamp of approval to many existing efforts. The goals and expectations of nanotechnology have been chosen in such a way that the march of the science and technology will yield new systems in many technological markets. There is little chance of disappointing the public (and Congress), due to the productivity of these endeavors. Yet, there appears to be more to the umbrella term than simply a new label for existing research directions. It has generated a new stimulus for academic pursuits in subtle ways that will have a lasting impact on our educational system.

Depth and Breadth a Bonus for Nanotechnology in Academia

University graduates must have skills in depth within a particular subject, a necessary aspect of pursuing the frontier of new knowledge with sufficient dedication to advance these frontiers. Yet, industry, concerned with satisfying consumers, is responsive to new opportunities that continually change. A university graduate may offer just what a given industrial position desires at a given time, but inevitable change may render those skills obsolete. Choosing new research directions more often, even within academic endeavors, is an inevitable part of a world characterized by rapidly expanding frontiers of new knowledge. *Depth* is an essential ingredient in the university experience, but *breadth* provides for greater flexibility when change occurs. The challenge to academia is to retain its strength in creating new knowledge while offering increasingly important breadth in its educational programs. Pursued separately, adding breadth to a student's experience can be satisfied by extending the time on campus, but this is costly and not particularly productive towards developing new knowledge, one of the primary goals of academia. Both professors and students are reluctant to substitute nondisciplinary courses in a curriculum already heavily laden with disciplinary material. What would be ideal in the academic experience would be to introduce *breadth* while simultaneously pursuing *depth*.

The subject of nanotechnology offers this opportunity, due to the multidisciplinary nature of the field. Researcher #1 in the field of chemistry or physics, for example, may wish to obtain knowledge of the structure of self-assembled particles, which may be of interest to researcher #2 in the field of electronics, who is interested in examining ways to fabricate quantum dots or novel structures for transistors. This is but one small example of the many opportunities that arise for joint objectives bridging disciplines. Such opportunities are labeled "nano-niches." These situations offer the student not only the opportunity to examine a phenomenon in depth, but to exchange results with similar activities in neighboring fields, where new perspectives may be obtained about other disciplines with relatively little additional effort (see schematic in Figure F.1).

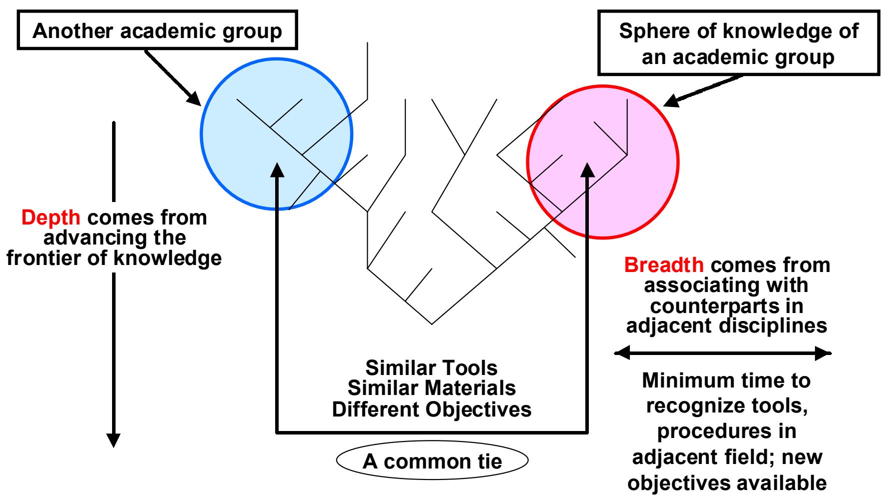

Figure F.1. Nanotechnology offers hope of depth plus breadth.

The value of multidisciplinary research has been extolled for years. However, it is impossible to have multidisciplinary research without having disciplines! Organizational changes that universities are now introducing include structures that encourage multidisciplinary pursuits, with consequent benefits to the student and the educational process. Breadth may be introduced by pursuing research objectives that have common features across disciplinary lines and by associating with more than one discipline. By encouraging "social interaction" (use of common instrumentation, materials, and theory) with peers in neighboring disciplines, the related frontiers in other disciplines may be easily introduced. This provides a graduate with stronger career opportunities, having the combined ability to pursue research in depth, but also having the ability to recognize additional options when the inevitable need for alternate opportunities arises.

Sharing expensive instrumentation in a common facility is one way to stimulate overlap of the academic disciplines, and this has been introduced extensively for nanotechnology. The National Nanofabrication Users Network (http://www.nnun.org/) consists of instrumentation centers at five major universities. A number of centers and institutes (http://www.nano.gov/centers.htm) have been introduced that stimulate the overlap of disciplines pursuing common goals. These organizations focus on objectives such as chemical and biological sensors, electron transport in molecules, nanoelectronics, assembly of nanostructures, and nanoscale devices/systems and their applications. These "academic nano-niches" are already established, and they will generate the benefits of multidisciplinary programs, with the concurrent advantages of depth and breadth. Other means of stimulating overlap involves common courses, seminars, and temporary exchanges of personnel.

Vision in Nanotechnology: How to Achieve it

One virtue of multidisciplinary research is the introduction of more comprehensive goals that may be achieved by several interactive research programs. A statement of these goals, along with the consequences, is frequently referred to as "vision." Occasionally, a research group sets out to conquer the larger goals with approaches that worked well with the previous in-depth methodology alone. That is, they pursue a larger goal with limited knowledge of the full picture. With the urgent need for faculty to obtain research funds, less time is available to examine the full picture associated with some of these larger goals. Some directions chosen by groups with a limited perspective may ignore the wisdom of more experienced communities. This problem is more severe when goals include "legions" of researchers from many disciplines, such as those currently being pursued by the computer industry.

Thus, the call for vision has generated its own unease in the midst of these transformations. Articulating a vision is tricky. As Yogi Berra stated, "*It's tough to make predictions, especially about the future*" (http://www.workinghumor.com/quotes/yogi_berra.shtml). This difficulty has been exacerbated by the introduction of virtual reality. Images can be readily drawn that conjure phenomena totally inconsistent with the world of reality. When applied to apparent scientific problems, misperceptions may result in groups expounding concepts they do not understand; perceptions may even violate the usual laws of physics (or related constraints recognized through years of experience).

Nevertheless, vision statements are important for the research world, and Congressional appropriations for research are increasingly tied to (1) a linear extrapolation of past success, and (2) visions that portend significant impact for the nation. The concepts associated with nanotechnology support these criteria in many ways. Most notably, enhanced electronics, enhanced medical diagnostics, improved medical procedures, and new materials are major areas that meet these two criteria. Stating a goal, pursuing it, and reaching it generate credibility. This is achieved best by those well versed in scientific principals and methods and the ramifications of potential paths to be pursued. It is not achieved by visionaries who appear to understand the world only through the images of virtual reality, without the sound knowledge of the basic principals drawn from the experimental world and experience with the perversity of Mother Nature. In addition, although serendipity has its place, it is not to be depended upon for productivity in research or for setting goals at the initiation of a program. The plethora of paths to follow in research exceeds by far the number of researchers. Consequently, a judicious choice of directions is essential, and the process of choosing these goals is vitally important to the health of the enterprise.

In light of the controversy surrounding discussion of the hazards of the so-called "self-replicating nanobots" (Tolles 2001, 173), a few words of caution seem in order. The nanotechnology community should show some restraint when releasing articles to the press about any major impact on an already established field. Setting scientific goals that may be achieved within a career (or within a decade) seems preferable to choosing goals that appear incompatible with the behavior of the physical world. The hazards of the so-called "self-replicating nanobots" seem to have already generated far more discussion than they warrant (Tolles 2001). Visions of ultra-fast and powerful computers the size of poppy seeds conjure unrealistic expectations, feeding further the fears that the products of our creation may be smarter than we are, and that we may sow the seeds of our own destruction. *"The rub in exploring the borderlands is finding that balance between being open-minded enough to accept radical new ideas but not so open-minded that your brains fall out"* (Shermer 2001, 29). We must recognize that it is difficult to predict the future; in particular, there is no reason to raise hopes for a device or a phenomenon that violates the basic laws of physics and chemistry. Another perspective: "*... the burden of proof is not on those who know how to make chips with* 10^7 *transistors and connect them together with millions of wires, it is up to those who show something in a laboratory to prove that it is better*" (Keyes 2001b).

The Academic Nano-Niches

Several "nano-niches" that appear most obvious today are outlined below. There are, of course, many other concepts emerging from the fertile frontier of miniaturization that are not easily categorized. Perhaps other significant niches will emerge in this new dimension of material control and behavior.

Nano-Niche #1

Objectives for enhancing electronic devices have been the basis for many nanotechnology programs. The nanotechnology efforts in programs such as molecular electronics have been pursued for decades with little impact on the electronics industry thus far. The more conservative microelectronics industry continues to pursue CMOS and is skeptical of radically new ideas that may deviate from its International Technology Roadmap for Semiconductors (ITRS) (Semiconductor Industry Association 2001) for a number of years in the future (Glimmell 2001). This is one area of nanotechnology that could benefit from a significant overlap with expertise in the electronics and information technology communities. Goals of forming molecular computers have appeared in a number of places. The physical realities one must meet to achieve such goals have been mentioned in a number of papers (e.g., Keyes 2001a; Meindl 1995, 1996; Meindl, Chen, and Davis 2001; Semiconductor Industry Association 2001). Molecular transistors have recently been fabricated (Bachtold et al. 2001; Schön, Meng, and Bao 2001). They have even been incorporated into circuits that can be used for logic operations (Bachtold et al. 2001). The challenges facing this nano-community now are very similar to those facing the semiconductor industry (see the Roadmap). These two communities will begin to work together cooperatively for a common goal. Innovative methods for incorporating new nanostructures into more conventional circuits will probably be the outcome of these interactions. The chemical and biological influences on the nanostructure of semiconductors is just beginning to be recognized (Whaley et al. 2000). Of course, alternative architectures for computational tasks represent a likely path for new breakthroughs. The brain of living species represents proof that such alternative architectures exist. It is through the innovation of these communities that such advances are likely to be introduced.

Nano-Niche #2

Research in nanostructures associated with biomolecular science is well recognized and proves to be a fertile field for a nano-niche. Biomolecules are often large and qualify as "nanostructures." Introduction of the tools and experience of chemists and physicists, even electrical engineers, in pursuing this mainstream of nanotechnology offers many opportunities for the synergism of multidisciplinary research in biology, biotechnology, and medicine. A biology student pursuing research with the tools of nanotechnology enters biomedical frontiers that include ability to fabricate sensors for the rapid, inexpensive detection of environmental hazards and disease organisms and to fabricate biomolecules with an objective to target selective cells (such as cancer cells) for modification of their function (Alivisatos 2001). Miniature chemistry laboratories are being fabricated on chips. These tools are likely to find applications in the task of sequencing genetic codes, of importance for medical purposes. This nano-niche includes the disciplines of chemistry, physics, biomolecular engineering, and even electrical engineering. One caution is worth noting. The ability to create new microbes, viruses, etc., in this field could lead to new biological species that present risks. As stated elsewhere, "The main risks for negative societal implications of nanotechnology will probably continue to be in the area of biotechnology rather than electronics" (Doering 2001, 68).

Nano-Niche #3

The field of materials science has always been a multidisciplinary endeavor. This is no less true for materials composed of nanostructures. One recent article points out the value of porous silicon as a stimulus to educational opportunities in electronics, optoelectronics, microoptics, sensors, solar cells, micromachining, acoustics, medicine, biotechnology, and astrophysics (Parkhutik and Canham 2000). A new material may be prepared using a variety of fabrication techniques from a number of disciplines and find applications in a number of technologies, accounting for the value of such a field for introducing breadth to the student experience. Of course, the depth from such an endeavor comes from advancing the knowledge about a given material using the tools from various scientific disciplines. Since new materials are of interest due to the possible substitution in an existing science or technology, the multidisciplinary aspect of materials will always exist.

Nanotechnology as a Stimulus to Inquiring Minds

As a stimulus for education in the sciences, nanotechnology has led to a wealth of fascinating scientific revelations. Attracting young inquiring minds has been the subject of an NSF-supported consortium project at Arizona State University in conjunction with other universities. This project, Interactive Nano-Visualization in Science and Engineering Education (IN-VSEE), may be viewed at http://invsee.asu.edu/. The goal of this program is to bring the excitement of discovery with electron and scanning tunneling microscopy into the classroom, targeting students in upper-level high school through college. At this level, the attraction of the multidisciplinary aspects is obvious. The subject of nanotechnology as a basis to illustrate scientific principals is likewise clear.

Summary

In summary, nanotechnology provides an impetus for transforming the academic experience, introducing a new stimulus for breadth in the career of a student while minimizing the additional time to assimilate that breadth. The historical functions of creating new knowledge through in-depth study need not be compromised with such programs. Programs in nanotechnology represent excellent areas of research to demonstrate this and will be one basis for a subtle transformation of the academic environment. Philosophers, business schools, psychologists, and many of the "soft sciences" may debate the implications of nanotechnology. However, without a realistic view of what may be expected from this fertile research frontier, there may be unnecessary discussions about unrealistic expectations. Information released to the media and studies of a social nature should follow careful assessments by technically qualified research teams presenting rational projections for the future potential of this fascinating field.

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UNIFYING PRINCIPLES IN COMPLEX SYSTEMS

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The ability of science and technology to augment human performance depends on an understanding of systems, not just components. The convergence of technologies is an essential aspect of the effort to enable functioning systems that include human beings and technology, serving the human beings to enhance their well-being directly and indirectly through what they do and what they do for other human beings. The recognition today that human beings function in teams rather than as individuals implies that technological efforts are essential that integrate human beings across scales of tools, communication, and biological and cognitive function.

Understanding the role of complex systems concepts in technology integration requires a perspective on how the concept of complexity is affecting science, engineering, and finally, technology integration.

Complex Systems and Science

The structure of scientific inquiry is being challenged by the broad relevance of complexity to the understanding of physical, biological, and social systems (Bar-Yam 2000; Bar-Yam and Minai 2002; Gallagher and Appenzeller 1999). Cross-disciplinary interactions are giving way to transdisciplinary and unified efforts to address the relevance of large amounts of information to describing, understanding, and controlling complex systems. From the study of biomolecular interactions (Service 1999; Normile 1999; Weng, Bhalla, and Iyengar 1999) to the strategy tactics of 21st century Information Age warfare and the war on terrorism, complexity has arisen as a unifying description of challenges to understanding and action. In this arena of complex systems, information, and action, structure and function are entangled. New approaches that recognize the importance of patterns of behavior, the multiscale space of possibilities, and evolutionary or adaptive processes that select systems or behaviors that can be effective in a complex world are central to advancing our understanding and capabilities (Bar-Yam 1997).

Complex Systems and Engineering

The failure of design and implementation of a new air traffic control system, failures of Intel processors, medical errors (IOM 2000), failures of medical drugs, even the failure of the Soviet Union, can be described as failures of large, complex systems. Systematic studies of large-scale engineering projects have revealed a remarkable proportion of failures in major high-investment projects. The precursors of such failures (multisystem integration, high-performance constraints, many functional demands, high rates of response, and large, context-specific protocols), are symptomatic of complex engineering projects. The methods for addressing and executing major engineering challenges must begin from the recognition of the role of complexity and the specific tools that can guide the design, or self-organization, of highly complex systems. Central to effective engineering are evaluation of the complexity of system functions; recognition of fundamental engineering tradeoffs of structure, function, complexity, and scale in system capabilities; and application of indirection to specification, design, and control of system development and the system itself.

Defining Complex Systems and Complex Tasks

One way to define a complex task is as a problem where the number of distinct possibilities that must be considered, anticipated, or dealt with is substantially larger than can be reasonably named or enumerated. We can casually consider in an explicit way tens of possibilities, a professional can readily deal with hundreds of possibilities, and a major project deals with thousands. The largest projects deal with tens of thousands. For larger numbers of possibilities, we must develop new strategies (Bar-Yam 1997). Simplifying a complex task by ignoring the need for different responses is what leads to errors or failures that affect the success of the entire effort, leaving it as a gamble with progressively higher risks.

The source of complex tasks is complex systems. Complex systems are systems with interdependent parts. Interdependence means that we cannot identify the system behavior by just considering each of the parts and combining them. Instead we must consider how the relationships between the parts affect the behavior of the whole. Thus, a complex task is also one for which many factors must be considered to determine the outcome of an action.

Converging Technologies

The rapid development of nanotechnology and its convergence with biological, information, and cognitive sciences is creating a context in which complex systems concepts that enable effective organizations to meet complex challenges can be realized through technological implementation. At the same time, complex systems concepts and methods can describe the framework in which this convergence is taking place. From the fine-scale control of systems based upon nanotechnology to understanding the system properties of the integrated socio-technical system consisting of human beings and computer information networks, the synergy of complex systems theory and converging technologies is apparent as soon as we consider the transition between components and functions.

Looking Forward

Human civilization, its various parts (including its technology), and its environmental context may be described as complex. The most reliable prediction possible is that this complexity will continue to increase. The great opportunity of the convergence of nanotechnology, biomedical, information, and cognitive sciences is an explosive increase in what is possible through combining advances in all areas. This is, by definition, an increase in the complexity of the systems that will be formed out of technology and of the resulting behaviors of people who use them directly or are affected by them. The increasing complexity suggests that there will be a growing need for widespread understanding of complex systems as a counterpoint to the increasing specialization of professions and professional knowledge. The insights of complex systems research and its methodologies may become pervasive in guiding what we build, how we build it, and how we use and live with it. Possibly the most visible outcome of these developments will be an improved ability of human beings, aided by technology, to address global social and environmental problems, third world development, poverty in developed countries, war, and natural disasters. At an intermediate scale, the key advances will dramatically change how individuals work together in forming functional teams that are more directly suited to the specific tasks they are performing. In the context of individual human performance, the key to major advances is recognizing that the convergence of technology will lead to the possibility of designing (or, more correctly, adapting) the environment of each individual for his or her individual needs and capabilities in play and work.

The Practical Need

Complex systems studies range from detailed studies of specific systems to studies of the mechanisms by which patterns of collective behaviors arise, to general studies of the principles of description and representation of complex systems. These studies are designed to enable us to understand and modify complex systems, design new ones for new functions, or create contexts in which they self-organize to serve our needs without direct design or specification. The need for applications to biological, cognitive, social, information, and other engineered systems is apparent.

Biology has followed an observational and reductionistic approach of accumulating large bodies of information about the parts of biological systems and looking for interpretations of system behavior in terms of these parts. It has become increasingly clear that biological systems are intricate, spatially structured, biochemically based networks. The role of information in biological action and the relationships of structure and function are only beginning to be probed by mathematicians, physicists, and engineers who are interested in biological systems as systems designed by nature for their functional capabilities. While biologists are increasingly looking to mathematical approaches and perspectives developed in physics and engineering, engineers are increasingly looking to biological systems for inspiration in designing artificial systems. Underlying these systems are a wealth of design principles in areas that include the biochemical networks (Gallagher and Appenzeller 1999; Service 1999; Normile 1999; Weng, Bhalla, and Iyengar 1999); immune systems (Perelson and Wiegel 1999; Noest 2000; Segel and Cohen 2001; Pierre et al. 1997) and neural systems (Anderson and Rosenfeld 1988; Bishop 1995; Kandel, Schwartz, and Jessell 2000); and animal behaviors such as the swimming mechanisms of fish (Triantafyllou and Triantafyllou 1995) and the gaits of animals (Golubitsky et al. 1999). These systems and architectures point to patterns of function that have a much higher robustness to failure and error and a higher adaptability than conventional human engineered systems.

Computers have made a transition from systems with tightly controlled inputs and outputs to systems that are networked and respond on demand as part of interactive information systems (Stein 1999). This has changed radically the nature of the issues facing their design. The collective behaviors of these networked computer systems, including the Internet, limit their effectiveness. Whether these have to do with the dynamics of packet loss in Internet traffic or the effect of computer viruses or worms (Forrest, Hofmeyr, and Somayaji 1997; Kephart et al. 1997; Goldberg et al. 1998), that at times have incapacitated a large fraction of the Internet, these effects are not small. The solution to these problems lies in understanding collective behaviors and in designing computer systems to be effective in environments with complex demands and to have higher defensive robustness.

The human brain is often considered the paradigmatic complex system. The implications of this recognition are that cognitive function is distributed within the brain, and mechanisms may vary from individual to individual. Complete explanations of cognitive function must themselves be highly complex. Major advances in cognitive science are currently slowed by a combination of efforts on the one hand to explain cognitive function directly from the behavior of individual molecular and cellular components, and on the other hand to aggregate or average the cognitive mechanisms of different human beings. Still, diverse advances that are being made are pointing the way to improvements in education (NIMH 2002), man-machine interfaces (Norman and Draper 1986; Nielsen 1993; Hutchins 1995), and retention of capabilities during aging (Stern and Carstensen 2000; Mandell and Schlesinger 1990; Davidson, Teicher, and Bar-Yam 1997).

The recognition of the complexity of conflict in the war on terrorism is another indication that the basic concept of complexity in social systems or problems has begun to be recognized. Unfortunately, this understanding has yet to be transferred to address other diverse major fundamental social system problems, as found in medical system cost containment, education system reform, and alleviation of poverty. In each case, current approaches continue to be dominated by large-scale strategies that are ineffective in addressing complex problems. Even with the appearance of more holistic approaches to, for example, third world development (World Bank 1998), the basic concept of existing strategy remains weakly informed by complex systems insights. This gap is an opportunity for major contributions by the field of complex systems at both the conceptual and technical levels. Further contributions can be made based upon research projects that emphasize the intrinsic complexity of these systems.

Understanding complex global physical and biological systems is also a major challenge. Many key problems today have to do with indirect effects of human activities that may have substantial destructive effects on the human condition. These include global warming and ecological deterioration due to overexploitation of resources. Effective approaches to these problems require understanding both the environmental and socioeconomic implications of our current actions and of actions that are designed to alleviate these problems (NSF n.d.). For example, the problem of global warming includes the effects of large-scale human activity interacting with both the linear and potentially nonlinear climactic response. Despite the grave risks associated with global warming, a key factor impeding actions to alleviate it is fear of major impacts of such efforts on socioeconomic systems. Better understanding of the potential effects of such interventions should enable considered actions to be taken.

Interest

Study of complex systems has become recognized as a basic scientific endeavor whose inquiry has relevance to the management of complex organizations in a complex world (Herz 2001). More specific attention has been gained in information technology (Horn 2001), biotechnology (Strausberg and Austin 1999; NSF n.d.; NIGMC n.d.; NSF 2001), healthcare industries, and the military.

Information technology companies building computer hardware and software have begun to recognize the inherently interactive and distributed nature of the systems they are designing. A significant example is the IBM "Autonomic Computing" initiative (Horn 2001), which is inspired by the biological paradigm of the autonomic nervous system and is conceptually based upon modeling robustness through biologically inspired system design. In a different perspective, Apple Computer has demonstrated the relevance of human factors, ranging from hardware design to ease-of-use and facilitation of creativity, as essential aspects of the role of computers in computer-human systems.

The major advances in biotechnology, including the genome project and other high-throughput data acquisition methods, have led to a dramatic growth in the importance of modeling and representation tools to capture large bodies of information and relate them to system descriptions and properties. Many private companies at the forefront of biotechnology are developing bioinformatics tools that strive to relate information to functional descriptions also described as "functional genomics" (Srausberg and Austin 1999). This is one facet of a broader recognition of the importance of capturing the multiscale properties of biological systems as reflected in NSF's biocomplexity initiative (NSF n.d.) and the complex biological systems programs at NIH (NIGMS 2002), as well as in joint programs.

For several years, the interest in complex systems as a conceptual and quantitative management tool has led consulting companies to work on practical implementations of strategy and more specific modeling efforts (Ernst and Young 2000, Gleick 1987). One of the areas of particular interest has been in the healthcare management community, where rapid organizational change has led to a keen interest in complex systems insights.

In the military and intelligence communities, there has been increasing realization of the relevance of networked distributed control and information systems. All branches of the military and the joint chiefs of staff have adopted vision statements that focus on complex systems concepts and insights as guiding the development of plans for information age warfare. These concepts affect both the engineering of military sensors, effectors, and information networks, and the underlying nature of military force command and control.

More broadly, the public's attention has been widely attracted to the description of complex systems research and insights. Indeed, many popular descriptions of complex systems research existed before the first textbook was written (Gleick 1987; Lewin 1992; Waldrop 1992; Gell-Mann 1994; Casti 1994; Goodwin 1994; Kauffman 1995; Holland 1995; Coveney and Highfield 1995; Bak 1996). The excitement of scientists as well as the public reflects the potential impact on our ability to understand questions that affect everyday life, perspectives on the world around us, fundamental philosophical disputes, and issues of public concern such as major societal challenges, the dynamics of social networks, global computer networks (the WWW), biomedical concerns, psychology, and ecology.

The Goals

The goals of complex systems research are to understand

- Understand the development and mechanisms of patterns of behavior and their use in engineering
- Understand the way to deal with complex problems (engineering, management, economic, sociopolitical) using strategies that relate the complexity of the challenge to the complexity of the system that must respond to them
- Understand the unifying principles of organization, particularly for systems that deal with large amounts of information (physical, biological, social, and engineered)
- Understand the interplay of behaviors at multiple scales and between the system and its environment

- Understand what is universal and what is not, when averaging applies and when it does not, what can be known and what cannot, what are the classes of universal behavior and the boundaries between them, and what are the relevant parameters for describing or affecting system behaviors
- Develop the ability to capture and represent specific systems rather than just accumulate data about them: (in this context) to describe relationships, know key behaviors, recognize relevance of properties to function, and simulate dynamics and response.
- Achieve a major educational shift toward unified understanding of systems and patterns of system behavior.

The traditional approach of science of taking things apart and assigning the properties of the system to its parts has been quite successful, but the limits of this approach have become apparent in recent years. When properties of a system result from dependencies and relationships but we assign them to their parts, major obstacles arise to understanding and control. Once the error of assignment is recognized, some of the obstacles can be overcome quickly, while others become subjects of substantive inquiry. Many scientists think that the parts are universal but the way parts work together is specific to each system. However, it has become increasingly clear that how parts work together can also be studied in general, and by doing so, we gain insight into every kind of system that exists, including physical systems like the weather as well as biological, social, and engineered systems.

Understanding complex systems does not mean that we can predict their behavior exactly; it is not just about massive databases or massive simulations, even though these are important tools of research in complex systems. The main role of research in the study of complex systems is that of recognizing what we can and cannot say about complex systems given a certain level (or scale) of description and knowing how we can generalize across diverse types of complex systems. It is just as important to know what we can know, as to know. Thus the concept of deterministic chaos appears to be a contradiction in terms: how can a deterministic system also be chaotic? It is possible because there is a rate at which the system behavior becomes dependent on finer and finer details (Cvitanovic 1989; Strogatz 1994; Ott 1993). Thus, how well we know a system at a particular time determines how well we can predict its behavior over time. Understanding complexity is neither about prediction or lack of predictability, but rather a quantitative knowledge of how well we can predict, and only within this constraint, what the prediction is.

Fundamental Research in Complex Systems: Theorems and Principles

Fundamental research in complex systems is designed to obtain characterizations of complex systems and relationships between quantities that characterize them. When there are well-defined relationships, these are formalized as theorems or principles. More general characterizations and classifications of complex systems are described below in major directions of inquiry. These are only a sample of the ongoing research areas.

A theorem or principle of complex systems should apply to physical, biological, social, and engineered systems. Similar to laws in physics, a law in complex systems should relate various quantities that characterize the system and its context. An example is Newton’s 2nd law that relates force, mass, and acceleration. Laws in complex systems relate qualities of system, action, environment, function, and information. Three examples follow.

Functional Complexity

Given a system whose function we want to specify, for which the environmental (input) variables have a complexity of $C(e)$, and the actions of the system have a complexity of $C(a)$, then the complexity of specification of the function of the system is

$$C(f)=C(a)\,2^{C(e)}$$

where complexity is defined as the logarithm (base 2) of the number of possibilities or, equivalently, the length of a description in bits.

The proof follows from recognizing that complete specification of the function is given by a table whose rows are the actions (C(a) bits) for each possible input, of which there are $2^{C(e)}$. Since no restriction has been assumed on the actions, all actions are possible, and this is the minimal length description of the function. Note that this theorem applies to the complexity of description as defined by the observer, so that each of the quantities can be defined by the desires of the observer for descriptive accuracy. This theorem is known in the study of Boolean functions (binary functions of binary variables) but is not widely understood as a basic theorem in complex systems (Bar-Yam 1997).

The implications of this theorem are widespread and significant to science and engineering. The exponential relationship between the complexity of function and the complexity of environmental variables implies that systems that have environmental variables (inputs) with more than a few bits (i.e., 100 bits or more of relevant input) have functional complexities that are greater than the number of atoms in a human being and thus cannot be reasonably specified. Since this is true about most systems that we characterize as "complex," the limitation is quite general. The implications are that fully phenomenological approaches to describing complex systems, such as the behaviorist approach to human psychology, cannot be successful. Similarly, the testing of response or behavioral descriptions of complex systems cannot be performed. This is relevant to various contexts, including testing computer chips, and the effects of medical drugs in double-blind population studies. In each case, the number of environmental variables (inputs) is large enough that all cases cannot be tested.

Requisite Variety

The Law of Requisite Variety states that the larger the variety of actions available to a control system, the larger the variety of perturbations it is able to compensate (Ashby 1957). Quantitatively, it specifies that a well-adapted system's probability of success in the context of its environment can be bounded:

$$-\mathrm{Log}_2(P) < C(e)-C(a)$$

Qualitatively, this theorem specifies the conditions in which success is possible: a matching between the environmental complexity and the system complexity, where success implies regulation of the impact of the environment on the system.

The implications of this theorem are widespread in relating the complexity of desired function to the complexity of the system that can succeed in the desired function. This is relevant to discussions of the limitations of specific engineered control system structures, of the limitations of human beings, and of human organizational structures.

Note that this theorem, as formulated, does not take into account the possibility of avoidance (actions that compensate for multiple perturbations because they anticipate and thus avoid the direct impact of the perturbations), or the relative measure of the space of success to that of the space of possibilities. These limitations can be compensated for.

Non-averaging

The Central Limit Theorem specifies that collective or aggregate properties of *independent* components with bounded probability distributions are Gaussian, distributed with a standard deviation that diminishes as the square root of the number of components. This simple solution to the collective behavior of non-interacting systems does not extend to the study of interacting or interdependent systems. The lack of averaging of properties of complex systems is a statement that can be used to guide the study of complex systems more generally. It also is related to a variety of other formal results, including Simpson's paradox (Simpson 1951), which describes the inability of averaged quantities to characterize the behavior of systems, and Arrow's Dictator Theorem, which describes the generic dynamics of voting systems (Arrow 1963; Meyer and Brown 1998).

The lack of validity of the Central Limit Theorem has many implications that affect experimental and theoretical treatments of complex systems. Many studies rely upon unjustified assumptions in averaging observations that lead to misleading, if not false, conclusions. Development of approaches that can identify the domain of validity of averaging and use more sophisticated approaches (like clustering) when they do not apply are essential to progress in the study of complex systems.

Another class of implications of the lack of validity of the Central Limit Theorem is the recognition of the importance of individual variations between different complex systems, even when they appear to be within a single class. An example mentioned above is the importance of individual differences and the lack of validity of averaging in cognitive science studies. While snowflakes are often acknowledged as individual, research on human beings often is based on assuming their homogeneity.

More generally, we see that the study of complex systems is concerned with their universal properties, and one of their universal properties is individual differences. This apparent paradox, one of many in complex systems (see below), reflects the importance of identifying when universality and common properties apply and when they do not, a key part of the study of complex systems.

Major Directions of Inquiry

How Understanding Self-Organization & Pattern Formation Can be Used to Form Engineered Systems

Self-organization is the process by which elements interact to create spatio-temporal patterns of behavior that are not directly imposed by external forces. To be concrete, consider the patterns of spontaneous traffic jams or heart beats. For engineering applications, the promise of understanding such pattern formation is the opportunity to use the natural dynamics of the system to create structures and impose functions rather than to construct them element by element. The robustness of self-organized systems is also a desired quality in conventional engineered systems — and on that is difficult to obtain. For biomedical applications, the promise is to understand developmental processes like the development of the fertilized egg into a complex physiological organism, like a human being. In the context of the formation of complex systems through development or through evolution, elementary patterns are the building blocks of complex systems. This is diametrically opposed to considering parts as the building blocks of such systems.

Spontaneous (self-organizing) patterns arise through symmetry breaking in a system when there are multiple inequivalent static or dynamic attractors. In general, in such systems, a particular element of a system is affected by forces from more than one other element, and this gives rise to "frustration" as elements respond to aggregate forces that are not the same as each force separately. Frustration contributes to the existence of multiple attractors and therefore of pattern formation.

Pattern formation can be understood using simple rules of local interaction, and there are identifiable classes of rules (universality) that give rise to classes of patterns. These models can be refined for more detailed studies. Useful illustrative examples of pattern forming processes are local-activation, long-range inhibition models that can describe patterns on animal skins, magnets, dynamics of air flows in clouds, wind-driven ocean waves, and swarm behaviors of insects and animals. Studies of spontaneous and persistent spatial pattern formation were initiated a half century ago by Turing (1952), and the wide applicability of patterns has gained increasing interest in recent years (Bar-Yam 1997; Meinhardt 1994; Murray 1989; Nijhout 1992; Segel 1984; Ball 1999).

The universality of patterns has been studied in statistical physics, where dynamic patterns arise in quenching to a first-order phase transition in cases of both conserved (spinodal decomposition, e.g., oil-water separation) and nonconserved (coarsening, e.g., freezing water) order parameters (Bray 1994) and also in growing systems (self-organized criticality, e.g., roughening). Generic types of patterns are relevant for such contexts and are distinguished by their spatio-temporal behaviors. Classic models have characteristic spatial scales (Turing patterns, coarsening, spinodal decomposition); others are scale invariant (self-organized criticality, roughening). Additional classes of complex patterns arise in networks with long-range interactions (rather than just spatially localized interactions) and are used for modeling spin glasses, neural networks (Anderson and Rosenfeld 1988; Bishop 1995; Kandel, Schwartz, and Jessell 2000), or genetic networks (Kauffman 1969).

Understanding Description and Representation

The study of how we describe complex systems is itself an essential part of the study of such systems. Since science is concerned with describing reproducible phenomena and engineering is concerned with the physical realization of described functions, description is essential to both. A description is some form of identified map of the actual system onto a mathematical or linguistic object. Shannon's information theory (Shannon 1963) has taught us that the notion of description is linked to the space of possibilities. Thus, while description appears to be very concrete, any description must reflect not only what is observed but also an understanding of what might be possible to see. An important practical objective is to capture information and create representations that allow human or computer-based inquiry into the properties of the system.

Among the essential concepts relevant to the study of description is the role of universality and non-universality (Wilson 1983) as a key to the classification of systems and of their possible representations. In this context, effective studies are those that identify the class of models that can capture properties of a system, rather than those of a single model of a system. Related to this issue is the problem of testability of representations through validating the mapping of the system to the representation. Finally, the practical objective of achieving human-usable representations must contend with the finite complexity of a human being, as well as other human factors due to both "intrinsic" properties of complex human function and "extrinsic" properties that are due to the specific environment in which human beings have developed their sensory and information processing systems.

The issue of human factors can be understood more generally as part of the problem of identifying the observer's role in description. A key issue is identifying the scale of observation: the level of detail that can be seen by an observer, or the degree of distinction between possibilities (NIGMS 2002; Bar-Yam 1997). Effective descriptions have a consistent precision so that all necessary but not a lot of unnecessary information is used, irrelevant details are eliminated, but all relevant details are included. A multiscale approach (Bar-Yam 1997) relates the notion of scale to the properties of the system and relates descriptions at different scales.

The key engineering challenge is to relate the characteristics of a description to function. This involves relating the space of possibilities of the system to the space of possibilities of the environment (variety, adaptive function). Complexity is a logarithmic measure of the number of possibilities of the system, equivalently the length of the description of a state. The Law of Requisite Variety (Ashby 1957) limits the possible functions of a system of a particular complexity.

Understanding Evolutionary Dynamics

The formation of complex systems and the structural/functional change of such systems, is the process of adaptation. Evolution (Darwin 1859) is the adaptation of populations through intergenerational changes in the composition of the population (the individuals of which it is formed), and learning is a similar process of adaptation of a system through changes in its internal patterns, including (but not exclusively) the changes in its component parts.

Characterizing the mechanism and process of adaptation, both evolution and learning, is a central part of complex systems research (Holland 1992; Kauffman 1993; Goodwin 1994; Kauffman 1995; Holland 1995). This research generalizes the problem of biological evolution by recognizing the relevance of processes of incremental change to the formation of all complex systems. It is diametrically opposed to the notion of creation in engineering that typically assumes new systems are invented without precursor. The reality of incremental changes in processes of creativity and design reflect the general applicability of evolutionary concepts to all complex systems.

The conventional notion of evolution of a population based upon replication with variation and selection with competition continues to be central. However, additional concepts have become recognized as important and are the subject of ongoing research, including the concepts of co-evolution (Kauffman 1993), ecosystems (Kauffman 1993), multiple niches, hierarchical or multilevel selection (Brandon and Burian 1984; Bar-Yam 2000), and spatial populations (Sayama, Kauffman, and Bar-Yam 2000). Ongoing areas of research include the traditional philosophical paradoxes involving selfishness and altruism (Sober and Wilson 1999), competition and cooperation (Axelrod 1984), and nature and nurture (Lewontin 20001). Another key area of ongoing inquiry is the origin of organization, including the origins of life (Day 1984), which investigate the initial processes that give rise to the evolutionary process of complex systems.

The engineering applications of evolutionary process are often mostly associated with the concept of evolutionary programming or genetic algorithms (Holland 1992; Fogel, Owens, and Walsh 1966). In this context, evolution is embodied in a computer. Among the other examples of the incorporation of evolution into engineering are the use of artificial selection and replication in molecular drug design (Herschlag and Cech 1990; Beaudry and Joyce 1992; Szostak 1999), and the human-induced variation with electronic replication of computer viruses, worms, and Trojan horses in Internet attacks (Goldberg et al. 1998). The importance of a wider application of evolution in management and engineering is becoming apparent. The essential concept is that evolutionary processes may enable us to form systems that are more complex than we can understand but will still serve functions that we need. When high complexity is necessary for desired function, the system should be designed for evolvability: e.g., smaller components (subdivided modular systems) evolve faster (Simon 1998). We note, however, that in addition to the usual concept of modularity, evolution should be understood to use patterns, not elements, as building blocks. The reason for this is that patterns are more directly related to collective system function and are therefore testable in a system context.

Understanding Choices and Anticipated Effects: Games and Agents

Game theory (von Neumann and Morgenstern 1944; Smith 1982; Fudenberg and Tirole 1991; Aumann and Hart 1992) explores the relationship between individual and collective action using models where there is a clear statement of consequences (individual payoffs), that depend on the actions of more than one individual. A paradigmatic game is the “prisoner’s dilemma.” Traditionally, game theory is based upon logical agents that make optimal decisions with full knowledge of the possible outcomes, though these assumptions can be usefully relaxed. Underlying game theory is the study of the role of anticipated effects on actions and the paradoxes that arise because of contingent anticipation by multiple anticipating agents, leading to choices that are undetermined within the narrow definition of the game and thus are sensitive to additional properties of the system. Game theory is relevant to fundamental studies of various aspects of collective behavior: altruism and selfishness, and cooperation and competition. It is relevant to our understanding of biological evolution, socio-economic systems, and societies of electronic agents. At some point in increasing complexity of games and agents, the models become agent-based models directed at understanding specific systems.

Understanding Generic Architectures

The concept of a network as capturing aspects of the connectivity, accessibility, or relatedness of components in a complex system is widely recognized as important in understanding aspects of these systems — so much so that many names of complex systems include the term “network.” Among the systems that have been identified thus are artificial and natural transportation networks (roads, railroads, waterways, airways) (Maritan et al. 1996; Banavar, Maritan, and Rinaldo 1999; Dodds and Rothman 2000), social networks (Wasserman and Faust 1994), military forces (INSS 1997), the Internet (Cheswick and Burch n.d.; Zegura, Calvert, and Donahoo 1997), the World Wide Web (Lawrence and Giles 1999; Huberman et al. 1998; Huberman and Lukose 1997), biochemical networks (Service 1999; Normile 1999; Weng, Bhalla, and Iyengar 1999), neural networks (Anderson and Rosenfeld 1988; Bishop 1995; Kandel, Schwartz, and Jessell 2000), and food webs (Williams and Martinez 2000). Networks are anchored by topological information about nodes and links, with additional information that can include nodal locations and state variables, link distances, capacities, and state variables, and possibly detailed local functional relationships involved in network behaviors.

In recent years, there has been significant interest in understanding the role played by the abstract topological structure of networks represented solely by nodes and links (Milgram 1967; Milgram 1992; Watts and Strogatz 1998; BarthÈlÈmy and Amaral 1999; Watts 1999; Latora and Marchiori 2001; Barab·si and Albert 1999; Albert, Jeong, and Barab·si 1999; Huberman and Adamic 1999; Albert, Jeong, and Barab·si 2000; Jeong et al. 2001). This work has focused on understanding the possible relationships between classes of topological networks and their functional capacities. Among the classes of networks contrasted recently are locally connected, random, small-world (Milgram 1967, 1992; Watts and Strogatz 1998; BarthÈlÈmy and Amaral 1999; Watts 1999), and scale-free networks (Latora and Marchiori 2001; Barab·si and Albert 1999; Albert, Jeong, and Barab·si 1999; Huberman and Adamic 1999; Albert, Jeong, and Barab·si 2000; Jeong et al. 2001). Other network architectures include regular lattices, trees, and hierarchically decomposable networks (Simon 1998). Among the issues of functional capacity are which networks are optimal by some measure, e.g., their efficiency in inducing connectivity, and the robustness or sensitivity of their properties to local or random failure or directed attack. The significance of these studies from an engineering perspective is in answering questions such as, What kind of organizational structure is needed to perform what function with what level of reliability? and What are the tradeoffs that are made in different network architectures? Determining the organizational structures and their tradeoffs is relevant to all scales and areas of the converging technologies: nanotechnology, biomedical, information, cognition, and social networks.

Understanding (Recognizing) the Paradoxes of Complex Systems

The study of complex systems often reveals difficulties with concepts that are used in the study of simpler systems. Among these are conceptual paradoxes. Many of these paradoxes take the form of the coexistence of properties that, in simpler contexts, appear to be incompatible. In some cases it has been argued that there is a specific balance of properties, for example the “edge-of-chaos” concept suggests a specific balance of order and chaos. However, in complex systems, order and chaos often coexist, and this is only one example of the wealth of paradoxes that are present. A more complete list would include paired properties such as the following:

- Stable and adaptable
- Reliable and controllable
- Persistent and dynamic
- Deterministic and chaotic
- Random and predictable
- Ordered and disordered
- Cooperative and competitive
- Selfish and altruistic
- Logical and paradoxical
- Averaging and non-averaging
- Universal and unique

While these pairs describe paradoxes of properties, the most direct paradox in complex systems is a recognition that more than one "cause" can exist, so that A causes B, and C causes B are not mutually incompatible statements. The key to understanding paradox in complex systems is to broaden our ability to conceive of the diversity of possibilities, both for our understanding of science, and for our ability to design engineered systems that serve specific functions and have distinct design tradeoffs that do not fit within conventional perspectives.

Developing Systematic Methodologies for the Study of Complex Systems

While there exists a conventional "scientific method," study of complex systems suggests that many more detailed aspects of scientific inquiry can be formalized. The existence of a unified understanding of patterns, description, and evolution as relevant to the study of complex systems suggests that we adopt a more systematic approach to scientific inquiry. Components of such a systematic approach would include experimental, theoretical, modeling, simulation, and analysis strategies. Among the aspects of a systematic strategy are the capture of quantitative descriptions of structure and dynamics, network analysis, dynamic response, information flow, multiscale decomposition, identification of modeling universality class, and refinement of modeling and simulations.

Major Application Areas of Complex Systems Research

The following should provide a sense of the integral nature of complex systems to advances in nanotechnology, biomedicine, information technology, cognitive science, and social and global systems. A level of complexity is found in their convergence.

Nanotechnology

Development of functional systems based on nanotechnological control is a major challenge beyond the creation of single elements. Indeed, the success of nanotechnology in controlling small elements can synergize well with the study of complex systems. To understand the significance of complex systems for nanotechnology, it is helpful to consider the smallest class of biological machines, also considered the smallest complex systems — proteins (Fersht 1999). Proteins are a marvel of engineering for design and manufacture. They also have many useful qualities that are not common in artificial systems, including robustness and adaptability through selection. The process of manufacturing a protein is divided into two parts, the creation of the molecular chain and the collapse of this chain to the functional form of the protein. The first step is ideal from a manufacturing point of view, since it enables direct manufacture from the template (RNA), which is derived from the information archive (DNA), which contains encoded descriptions of the protein chain. However, the chain that is formed in manufacture is not the functional form. The protein chain "self-organizes" (sometimes with assistance from other proteins) into its functional (folded) form. By manufacturing proteins in a form that is not the functional form, key aspects of the manufacturing process can be simplified, standardized, and made efficient while allowing a large variety of functional machines described in a simple language. The replication of DNA provides a mechanism of creating many equivalent information archives (by exponential growth) that can be transcribed to create templates to manufacture proteins in a massively parallel way when mass production is necessary. All of these processes rely upon rapid molecular dynamics. While proteins are functionally robust in any particular function, their functions can also be changed or adapted by changing the archive, which "describes" their function, but in an indirect and non-obvious way. The rapid parallel process of creation of proteins allows adaptation of new machines through large-scale variation and selection.

A good example of this process is found in the immune system response (Perelson and Wiegel 1999; Noest 2000; Segel and Cohen 2001; Pierre et al. 1997). The immune system maintains a large number of different proteins that serve as antibodies that can attach themselves to harmful antigens. When there is an infection, the antigens that attach most effectively are replicated in large numbers, and they are also subjected to a process of accelerated evolution through mutation and selection that generates even better-suited antibodies. Since this is not the evolutionary process of organisms, it is, in a sense, an artificial evolutionary process optimized (engineered) for the purpose of creating well-adapted proteins (machines). Antibodies are released into the blood as free molecules, but they are also used as tools by cells that hold them attached to their membranes so that the cells can attach to, "grab hold of," antigens. Finally, proteins also form complexes, are part of membranes and biochemical networks, showing how larger functional structures can be built out of simple machines. An artificial analog of the immune system's use of evolutionary dynamics is the development of ribozymes by *in vitro* selection, now being used for drug design (Herschlag and Cech 1990; Beaudry and Joyce 1992; Szostak 1999).

Proteins and ribozymes illustrate the crossover of biology and nanotechnology. They also illustrate how complex systems concepts of self-organization, description, and evolution are important to nanotechnology. Nanotechnological design and manufacturing may take advantage of the system of manufacture of proteins or other approaches may be used. Either way, the key insights of how proteins work shows the importance of understanding various forms of description (DNA); self-reproduction of the manufacturing equipment (DNA replication by polymerase chain reaction or cell replication); rapid template-based manufacture (RNA transcription to an amino-acid chain); self-organization into functional form (protein folding); and evolutionary adaptation through replication (mutation of DNA and selection of protein function) and modular construction (protein complexes). Understanding complex systems concepts thus will enable the development of practical approaches to nanotechnological design and manufacture and to adaptation to functional requirements of nanotechnological constructs.

Biomedical Systems

At the current time, the most direct large-scale application of complex systems methods is to the study of biochemical networks (gene regulatory networks, metabolic networks) that reveal the functioning of cells and the possibilities of medical intervention (Service 1999; Normile 1999; Weng, Bhalla and Iyengar 1999). The general studies of network structure described above are complementary to detailed studies of the mechanisms and function of specific biochemical systems (von Dassow et al. 2001). High-throughput data acquisition in genomics and proteomics is providing the impetus for constructing functional descriptions of biological systems (Strausberg and Austin 1999). This, however, is only the surface of the necessary applications of complex systems approaches that are intrinsic to the modern effort to understand biological organisms, their relationships to each other, and their relationship to evolutionary history. The key to a wider perspective is recognizing that the large quantities of data that currently are being collected are being organized into databases that reflect the data acquisition process rather than the potential use of this information. Opportunities for progress will grow dramatically when the information is organized in a form that provides a description of systems and system functions. Since cellular and multicellular organisms, including the human being, are not simply biochemical soups, this description must capture the spatiotemporal dynamics of the system as well as the biochemical network and its dynamics. In the context of describing human physiology from the molecular scale, researchers at the Oak Ridge National Laboratory working towards this goal call it the Virtual Human Project (Appleton 2000). This term has also been used to describe static images of a particular person at a particular time (NLM 2002).

The program of study of complex systems in biology requires not only the study of a particular organism (the human being) or a limited set of model organisms, as has been done in the context of genomics until now. The problem is to develop comparative studies of systems, understanding the variety that exists within a particular type of organism (e.g., among human beings) and the variety that exists across types of organisms. Ultimately, the purpose is to develop an understanding or description of the patterns of biological systems today as well as throughout the evolutionary process. The objective of understanding variety and evolution requires us to understand not just any particular biochemical system, but the space of possible biochemical systems filtered to the space of those that are found today, their general properties, their specific mechanisms, how these general properties carry across organisms, and how they are modified for different contexts. Moreover, new approaches that consider biological organisms through the relationship of structure and function, and through information flow are necessary to this understanding.

Increasing knowledge about biological systems is providing us with engineering opportunities and hazards. The great promise of our biotechnology is unrealizable without a better understanding of the systematic implications of interventions that we can do today. The frequent appearance of biotechnology in the popular press through objections to genetic engineering and cloning reveals the great specific knowledge and the limited systemic knowledge of these systems. The example of corn genetically modified for feed and its subsequent appearance in corn eaten by human beings (Quist and Chapela 2001) reveals the limited knowledge we have of indirect effects in biological systems. This is not a call to limit our efforts, simply to focus on approaches that emphasize the roles of indirect effects and explore their implications scientifically. Without such studies, not only are we shooting in the dark, but in addition we will be at the mercy of popular viewpoints.

Completion of the virtual human project would be a major advance toward creating models for medical intervention. Such models are necessary when it is impossible to test multidrug therapies or specialized therapies based upon individual genetic differences. Intervention in complex biological systems is an intricate problem. The narrow bridge that currently exists between medical double blind experiments and the large space of possible medical interventions can be greatly broadened through systemic models that reveal the functioning of cellular systems and their relationship to cellular function. While today individual medical drugs are tested statistically, the main fruit of models will be

- to reveal the relationship between the function of different chemicals and the possibility of multiple different types of interventions that can achieve similar outcomes
- the possibility of discovering small variations in treatment that can affect the system differently
- possibly most importantly, to reveal the role of variations between human beings in the difference of response to medical treatment

A key aspect of all of these is the development of complex systems representations of biological function that reveal the interdependence of biological system and function.

Indeed, the rapid development of medical technologies and the expectation of even more dramatic changes should provide an opportunity for, even require, a change in the culture of medical practice. Key to these changes should be understanding of the dynamic state of health. Conventional *homeostatic* perspectives on health are being modified to *homeodynamic* perspectives (Goldberger, Rigney, and West 1990; Lipsitz and Goldberger 1992). What is needed is a better understanding of the functional capabilities of a healthy individual to respond to changes in the external and internal environment for self-repair or -regulation. This is essential to enhance the individual's capability of maintaining his or her own health. For example, while physical decline is a problem associated with old age, it is known that repair and regulatory mechanisms begin to slow down earlier, e.g., in the upper 30s, when professional athletes typically end their careers. By studying the dynamic response of an individual and changes over his/her life cycle, it should be possible to understand these early aspects of aging and to develop interventions that maintain a higher standard of health. More generally, understanding of the network of regulatory and repair mechanisms should provide a better mechanism for dynamic monitoring — with biomedical sensors and imaging — health and disease and the impact of medical interventions. This would provide key information about the effectiveness of interventions for each individual, enabling feedback into the treatment process that can greatly enhance its reliability.

Information Systems

Various concepts have been advanced over the years for the importance of computers in performing large-scale computations or in replacing human beings through artificial intelligence. Today, the most apparent role of computers is as personal assistants and as communication devices and information archives for the socioeconomic network of human beings. The system of human beings and the Internet has become an integrated whole leading to a more intimately linked system. Less visibly, embedded computer systems are performing various specific functions in information processing for industrial age devices like cars. The functioning of the Internet and the possibility of future networking of embedded systems reflects the properties of the network as well as the properties of the complex demands upon it. While the Internet has some features that are designed, others are self-organizing, and the dynamic behaviors of the Internet reflect problems that may be better solved by using more concepts from complex systems that relate to interacting systems adapting in complex environments rather than conventional engineering design approaches.

Information systems that are being planned for business, government, military, medical, and other functions are currently in a schizophrenic state where it is not clear whether distributed intranets or integrated centralized databases will best suit function. While complex systems approaches generally suggest that creating centralized databases is often a poor choice in the context of complex function, the specific contexts and degree to which centralization is useful must be understood more carefully in terms of their functions and capabilities, both now and in the future (Bar-Yam 2001).

A major current priority is enabling computers to automatically configure themselves and carry out maintenance without human intervention (Horn 2001). Currently, computer networks are manually configured, and often the role of various choices in configuring them are not clear, especially for the performance of networks. Indeed, evidence indicates that network system performance can be changed dramatically using settings that are not recognized by the users or system administrators until chance brings them to their attention. The idea of developing more automatic processes is a small part of the more general perspective of developing adaptive information systems. This extends the concept of self-configuring and self-maintenance to endowing computer-based information systems with the ability to function effectively in diverse and variable environments. In order for this functioning to take place, information systems must, themselves, be able to recognize patterns of behavior in the demands upon them and in their own activity. This is a clear direction for development of both computer networks and embedded systems.

Development of adaptive information systems in networks involves the appearance of software agents. Such agents range from computer viruses to search engines and may have communication and functional capabilities that allow social interactions between them. In the virtual world, complex systems perspectives are imperative in considering such societies of agents. As only one example, the analogy of software agents to viruses and worms has also led to an immune system perspective in the design of adaptive responses (Forrest, Hofmeyr, and Somayaji 1997; Kephart et al. 1997).

While the information system as a system is an important application of complex systems concepts, complex systems concepts also are relevant to considering the problem of developing information systems as effective repositories of information for human use. This involves two aspects, the first of which is the development of repositories that contain descriptions of complex systems that human beings would like to understand. The example of biological databases in the previous section is only one example. Other examples are socio-economic systems, global systems, and astrophysical systems. In each case, the key issue is to gain an understanding of how such complex systems can be effectively represented. The second aspect of designing such information repositories is the recognition of human factors in the development of human-computer interfaces (Norman and Draper 1986; Nielsen 1993; Hutchins 1995). This is important in developing all aspects of computer-based information systems, which are used by human beings and designed explicitly or implicitly to serve human beings.

More broadly, the networked information system that is being developed serves as part of the human socio-economic-technological system. Various parts of this system, which includes human beings and information systems, as well as the system as a whole, are functional systems. The development and design of this self-organizing system and the role of science and technology is a clear area of application of complex systems understanding and methods. Since this is a functional system based upon a large amount of information, among the key questions is how should the system be organized when action and information are entangled.

Cognitive Systems

The decade of the 1990s was declared by President George Bush, senior (1990), the “decade of the brain,” based, in part, on optimism that new experimental techniques such as Positron Emission Tomography (PET) imaging would provide a wealth of insights into the mechanisms of brain function. However, a comparison of the current experimental observations of cognitive processes with those of biochemical processes of gene expression patterns reveals the limitations that are still present in these observational techniques in studying the complex function of the brain. Indeed, it is reasonable to argue that the activity of neurons of a human being and their functional assignment is no less complex than the expression of genes of a single human cell.

Current experiments on gene expression patterns allow the possibility of knocking out individual genes to investigate the effect of each gene on the expression pattern of all other genes measured individually. The analogous capability in the context of cognitive function would be to incapacitate an individual neuron and investigate the effect on the firing patterns of all other neurons individually. Instead, neural studies are based upon sensory stimulation and measures of the average activity of large regions of cells. In gene expression studies, many cells are used with the same genome and a controlled history through replication, and averages are taken of the behavior of these cells. In contrast, in neural studies averages are often taken of the activity patterns of many individuals with distinct genetic and environmental backgrounds. The analogous biochemical experiment would be to average behavior of many cells of different types from a human body (muscle, bone, nerve, red blood cell, etc.) and different individuals, to obtain a single conclusion about the functional role of the genes.

The more precise and larger quantities of genome data have revealed the difficulties in understanding genomic function and the realization that gene function must be understood through models of genetic networks (Fuhrman et al. 1998). This is to be contrasted with the conclusions of cognitive studies that investigate the aggregate response of many individuals to large-scale sensory stimuli and infer functional assignments. Moreover, these functional assignments often have limited independently verifiable or falsifiable implications. More generally, a complex systems perspective suggests that it is necessary to recognize the limitations of the assignment of function to individual components ranging from molecules to subdivisions of the brain; the limitations of narrow perspectives on the role of environmental and contextual effects that consider functioning to be independent of effects other than the experimental stimulus; and the limitations of expectations that human differences are small and therefore that averaged observations have meaning in describing human function.

The problem of understanding brain and mind can be understood quite generally through the role of relationships between patterns in the world and patterns of neuronal activity and synaptic change. While the physical and biological structure of the system is the brain, the properties of the patterns identify the psychofunctioning of the mind. The relationship of external and internal patterns are further augmented by relationships between patterns within the brain. The functional role of patterns is achieved through the ability of internal patterns to represent both concrete and abstract entities and processes, ranging from the process of sensory-motor response to internal dialog. This complex nonlinear dynamic system has a great richness of valid statements that can be made about it, but identifying an integrated understanding of the brain/mind system cannot be captured by perspectives that limit their approach through the particular methodologies of the researchers involved. Indeed, the potential contributions of the diverse approaches to studies of brain and mind have been limited by the internal dynamics of the many-factioned scientific and engineering approaches.

The study of complex systems aspects of cognitive systems, including the description of patterns in the world and patterns in mind, the construction of descriptions of complex systems, and the limitations on information processing that are possible for complex systems, are relevant to the application of cognitive studies to the understanding of human factors in man-machine systems (Norman and Draper 1986; Nielsen 1993; Hutchins 1995) and more generally to the design of systems that include both human beings and computer-based information systems as functional systems. Such hybrid systems, mentioned previously in the section on information technology, reflect the importance of the converging technology approach.

The opportunity for progress in understanding the function of the networked, distributed neuro-physiological system also opens the possibility of greater understanding of development, learning, and aging (NIMH n.d.; Stern and Carstensen 2000; Mandell and Schlesinger 1990; Davidson, Teicher, and Bar-Yam 1997). While the current policy of education reform is using a uniform measure of accomplishment and development through standardized testing, it is clear that more effective measures must be based on a better understanding of cognitive development and individual differences. The importance of gaining such knowledge is high because evaluation of the effectiveness of new approaches to education typically requires a generation to see the impact of large-scale educational changes on society. The positive or negative effects of finer-scale changes appear to be largely inaccessible to current research. Thus, we see the direct connection between complex systems approaches to cognitive science and societal policy in addressing the key challenge of the education system. This in turn is linked to solution of many other complex societal problems, including poverty, drugs and crime, and also to effective functioning of our complex economic system requiring individuals with diverse and highly specialized capabilities.

Studies of the process of aging are also revealing the key role of environment on the retention of effective cognitive function (Stern and Carstensen 2000; Mandell and Schlesinger 1990; Davidson, Teicher, and Bar-Yam 1997). The notion of "use it or lose it," similar to the role of muscular exercise, suggests that unused capabilities are lost more rapidly than used ones. While this is clearly a simplification, since losses are not uniform across all types of capabilities and overuse can also cause deterioration, it is a helpful guideline that must be expanded upon in future research. This suggests that research should focus on the effects of the physical and social environments for the elderly and the challenges that they are presented with.

We can unify and summarize the complex systems discussion of the cognitive role of the environment for children, adults, and the elderly by noting that the complexity of the environment and the individual must be matched for effective functioning. If the environment is too complex, confusion and failure result; if the environment is too simple, deterioration of functional capability results. One approach to visualizing this process is to consider that the internal physical parts and patterns of activity are undergoing evolutionary selection dictated by the patterns of activity that result from environmental stimulation. This evolutionary approach also is relevant to the recognition that individual differences are analogous to different ecological niches. A more detailed research effort would not only consider the role of complexity but also the effect of specific patterns of environment and patterns of internal functioning, individual differences in child development, aging, adult functioning in teams, and hybrid human-computer systems.

Social Systems and Societal Challenges

While social systems are highly complex, there are still relatively simple collective behaviors that are not well understood. These include commercial fads, market cycles and panics, bubbles and busts. Understanding the fluctuating dynamics and predictability of markets continues to be a major challenge. It is important to emphasize that complex systems studies are not necessarily about predicting the market, but about understanding its predictability or lack thereof.

More generally, there are many complex social challenges associated with complex social systems ranging from military challenges to school and education system failures, healthcare errors, and problems with quality of service. Moreover, other major challenges remain in our inability to address fundamental social ills such as poverty (in both developed and undeveloped countries), drug use, and crime. To clarify some aspects of social systems from a complex systems perspective, it is helpful to focus on one of these, and the current military context is a convenient focal point.

Wars are major challenges to our national abilities. The current war on terrorism is no exception. In dealing with this challenge, our leadership, including the president and the military, has recognized that this conflict is highly complex. Instead of just sending in tens to hundreds of thousands of troops, as was done in the Gulf War, there is a strategy of using small teams of special forces to gain intelligence and lay the groundwork for carefully targeted, limited and necessary force.

A large-scale challenge can be met by many individuals doing the same thing at the same time, or repeating the same action, similar to a large military force. In contrast, a complex challenge must be met by many individuals doing many different things at different times. Each action has to directly match the local task that must be done. The jungles of Vietnam and the mountains of Afghanistan, reported to have high mountains and deep narrow valleys, are case studies in complex terrains. War is complex when targets are hidden, not only in the terrain but also among people — bystanders or friends. It is also complex when the enemy can itself do many different things, when the targets are diverse, the actions that must be taken are specific, and the difference between right and wrong action is subtle.

While we are still focused on the war on terrorism, it seems worthwhile to transfer the lessons learned from different kinds of military conflicts to other areas where we are trying to solve major problems. Over the past 20 years, the notion of war has been used to describe the War on Poverty, the War on Drugs, and other national challenges. These were called wars because they were believed to be challenges requiring the large force of old-style wars. They are not. They are complex challenges that require detailed intelligence and the application of the necessary forces in the right places. Allocating large budgets for the War on Poverty did not eliminate the problem; neither does neglect. The War on Drugs has taken a few turns, but even the recent social campaign "Just say no!" is a large-scale approach. Despite positive intentions, we have not won these wars because we are using the wrong strategy.

There are other complex challenges that we have dealt with using large forces. Third World development is the international version of the War on Poverty to which the World Bank and other organizations have applied large forces. Recently, more thoughtful approaches are being taken, but they have not gone far enough. There is a tendency to fall into the "central planning trap." When challenges become complex enough, even the very notion of central planning and control fails. Building functioning socioeconomic systems around the world is such a complex problem that it will require many people taking small and targeted steps — like the special forces in Afghanistan.

There are other challenges that we have not yet labeled wars, which are also suffering from the same large-force approach. Among these are cost containment in the medical system and improving the education system. In the medical system, the practice of cost controls through managed care is a large-force approach that started in the early 1980s. Today, the medical system quality of care is disintegrating under the stresses and turbulence generated by this strategy. Medical treatment is clearly one of the most complex tasks we are regularly engaged in. Across-the-board cost control should not be expected to work. We are just beginning to apply the same kind of large-scale strategy to the education system through standardized testing. Here again, a complex systems perspective suggests that the outcomes will not be as positive as the intentions.

The wide applicability of lessons learned from fighting complex wars, and the effective strategies that resulted, should be further understood through research projects that can better articulate the relevant lessons and how they pertain to solving the many and diverse complex social problems we face.

Global and Larger Systems

Global systems — physical, biological, and social — are potentially the most complex systems that are studied by science today. Complex systems methods can provide tools for analyzing their large-scale behavior. Geophysical and geobiological systems, including meteorology, plate tectonics and earthquakes, river and drainage networks, the biosphere and ecology, have been the motivation for and the application of complex systems methods and approaches (Dodds and Rothman 2000; Lorenz 1963; Bak and Tang 1989; Rundle, Turcotte, and Klein 1996; NOAA 2002). Such applications also extend to other planetary, solar, and astrophysical systems. Converging technologies to improve human performance may benefit from these previous case studies.

Among the key problems in studies of global systems is understanding the indirect effects of global human activity, which in many ways has reached the scale of the entire earth and biosphere. The possibility of human impact on global systems through overexploitation or other by-products of industrial activity has become a growing socio-political concern. Of particular concern are the impacts of human activity on the global climate (climate change and global warming), on the self-sustaining properties of the biosphere through exploitation and depletion of key resources (e.g., food resources like fish, energy resources like petroleum, deforestation, loss of biodiversity). Other global systems include global societal problems that can include the possibility of global economic fluctuations, societal collapse, and terrorism. Our effectiveness in addressing these questions will require greater levels of understanding and representations of indirect effects, as well as knowledge of effective mechanisms for intervention, if necessary. In this context, the objective is to determine which aspects of a system can be understood or predicted based upon available information, along with the level of uncertainty in such predictions. In some cases, the determination of risk or uncertainty is as important as the prediction of the expected outcome. Indeed, knowing "what is the worst that can happen" is often an important starting point for effective decision-making.

In general, the ability of humanity to address global problems depends on the collective behavior of people around the world. Global action is now typical in response to local natural disasters (earthquakes, floods, volcanoes, droughts); man-made problems from wars (Gulf War, Bosnia, Rwanda, the war on terrorism); and environmental concerns (international agreements on environment and development). In addition, there is a different sense in which addressing global concerns requires the participation of many individuals: The high complexity of these problems implies that many individuals must be involved in addressing these problems, and they must be highly diverse and yet coordinated. Thus, the development of complex systems using convergent technologies that facilitate human productivity and cooperative human functioning will be necessary to meet these challenges.

What is to be Done?

The outline above of major areas of complex systems research and applications provides a broad view in which many specific projects should be pursued. We can, however, single out three tasks that, because of their importance or scope, are worth identifying as priorities for the upcoming years: (1) transform education; (2) develop sets of key system descriptions; and (3) design highly complex engineering projects as evolutionary systems.

Transform Education

The importance of education in complex systems concepts for all areas of science, technology, and society at large has been mentioned above but should be reemphasized. There is need for educational materials and programs that convey complex systems concepts and methods and are accessible to a wide range of individuals, as well as more specific materials and courses that explain their application in particular contexts. A major existing project on fractals can be used as an example (Buldyrev et al. n.d.). There are two compelling reasons for the importance of such projects. The first is the wide applicability of complex systems concepts in science, engineering, medicine, and management. The second is the great opportunity for engaging the public in exciting science with a natural relevance to daily life, and enhancing their support for ongoing and future research. Ultimately, the objective is to integrate complex systems concepts throughout the educational system.

Develop Sets of Key System Descriptions

There are various projects for describing specific complex systems (NOAA 2002; Kalra et al. 1988; Goto, Kshirsagar, and Magnenat-Thalmann 2001; Heudin 1999; Schaff et al. 1997; Tomita et al. 1999), ranging from the earth to a single cell, which have been making substantial progress. Some of these focus more on generative simulation, others on representation of observational data. The greatest challenge is to merge these approaches and develop system descriptions that identify both the limits of observational and modeling strategies, and the opportunities they provide jointly for the description of complex systems. From this perspective, some of the most exciting advances are in representation of human forms in computer-based animation (Kalra et al. 1988; Goto, Kshirsagar, and Magnenat-Thalmann 2001; Heudin 1999), and particularly, in projecting human beings electronically. Pattern recognition is performed on realtime video to obtain key information about dynamic facial expression and speech, which is transmitted electronically to enable animation of a realistic computer-generated image that represents, in real time, the facial expression and speech of the person at a remote location (Goto, Kshirsagar, and Magnenat-Thalmann 2001). Improvement in such systems is measured by the growing bandwidth necessary for the transmission, which reflects our inability to anticipate system behavior from prior information.

To advance this objective more broadly, developments in systematic approaches (including quantitative languages, multiscale representations, information capture, and visual interfaces) are necessary, in conjunction with a set of related complex systems models. For example, current computer-based tools are largely limited to separated procedural languages (broadly defined) and databases. A more effective approach may be to develop quantitative descriptive languages based on lexical databases that merge the strength of human language for description with computer capabilities for manipulating and visually representing quantitative attributes (Smith, Bar-Yam, and Gelbart 2001). Such extensible quantitative languages are a natural bridge between quantitative mathematics, physics, and engineering languages and qualitative lexicons that dominate description in biology, psychology, and social sciences. They would facilitate describing structure, dynamics, relationships, and functions better than, for example, graphical extensions of procedural languages. This and other core complex systems approaches should be used in the description of a set of key complex systems under a coordinating umbrella.

For each system, an intensive collection of information would feed a system representation whose development would be the subject and outcome of the project. For example, in order to develop a representation of a human being, there must be intensive collection of bio-psycho-social information about the person. This could include multisensor monitoring of the person's physical (motion), psycho-social (speech, eye-motion), physiological (heart rate), and biochemical (food and waste composition, blood chemistry) activity over a long period of time, with additional periodic biological imaging and psychological testing. Virtual world animation would be used to represent both the person and his/her environment. Models of biological and psychological function representing behavioral patterns would be incorporated and evaluated. Detailed studies of a particular individual along with comparative studies of several individuals would be made to determine both what is common and what is different. As novel relevant convergent technologies become available that would affect human performance or affect our ability to model human behavior, they can be incorporated into this study and evaluated. Similar coordinating projects would animate representations of the earth, life on earth, human civilization, a city, an animal's developing embryo, a cell, and an engineered system, as suggested above. Each such project is both a practical application and a direct test of the limits of our insight, knowledge, and capabilities. Success of the projects is guaranteed because their ultimate objective is to inform us about these limits.

Design Highly Complex Engineering Projects as Evolutionary Systems

The dramatic failures in large-scale engineering projects such as the Advanced Automation System (AAS), which was originally planned to modernize air traffic control, should be addressed by complex systems research. The AAS is possibly the largest engineering project to be abandoned. It is estimated that several billion dollars were spent on this project. Moreover, cost overruns and delays in modernization continue in sequel projects. One approach to solving this problem, simplifying the task definition, cannot serve when the task is truly complex, as it appears to be in this context. Instead, a major experiment should be carried out to evaluate implementation of an evolutionary strategy for large-scale engineering. In this approach, the actual air traffic control system would become an evolving system, including all elements of the system, hardware, software, the air traffic controllers, and the designers and manufacturers of the software and hardware. The system context would be changed to enable incremental changes in various parts of the system and an evolutionary perspective on population change.

The major obstacle to any change in the air traffic control system is the concern for safety of airplanes and passengers, since the existing system, while not ideally functioning, is well tested. The key to enabling change in this system is to introduce redundancy that enables security while allowing change. For example, in the central case of changes in the air traffic control stations, the evolutionary process would use "trainers" that consist of doubled air traffic control stations, where one has override capability over the other. In this case, rather than an experienced and inexperienced controller, the two stations are formed of a conventional and a modified station. The modified station can incorporate changes in software or hardware. Testing can go on as part of operations, without creating undue risks. With a large number of trainers, various tests can be performed simultaneously and for a large number of conditions. As a particular system modification becomes more extensively tested and is found to be both effective and reliable, it can be propagated to other trainers, even though testing would continue for extended periods of time. While the cost of populating multiple trainers would appear to be high, the alternatives have already been demonstrated to be both expensive and unsuccessful. The analogy with paired chromosomes in DNA can be seen to reflect the same design principle of redundancy and robustness. These brief paragraphs are not sufficient to explain the full evolutionary context, but they do resolve the key issue of safety and point out the opening that this provides for change. Such evolutionary processes are also being considered for guiding other large-scale engineering modernization programs (Bar-Yam 2001).

Conclusions

The excitement that is currently felt in the study of complex systems arises not from a complete set of answers but rather from the appearance of a new set of questions, which are relevant to NBIC. These questions differ from the conventional approaches to science and technology and provide an opportunity to make major advances in our understanding and in applications.

The importance of complex systems ideas in technology begins through recognition that novel technologies promise to enable us to create ever more complex systems. Even graphics-oriented languages like OpenGL are based on a procedural approach to drawing objects rather than representing them. Moreover, the conventional boundary between technology and the human beings that use them is not a useful approach to thinking about complex systems of human beings and technology. For example, computers as computational tools have given way to information technology as an active interface between human beings that are working in collaboration. This is now changing again to the recognition that human beings and information technology are working together as an integrated system.

More generally, a complex systems framework provides a way in which we can understand how the planning, design, engineering, and control over simple systems gives way to new approaches that enable such systems to arise and be understood with limited or indirect planning or control. Moreover, it provides a way to better understand and intervene (using technology) in complex biological and social systems.

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MIND OVER MATTER IN AN ERA OF CONVERGENT TECHNOLOGIES

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Within the next 10 to 15 years, economically viable activities connected with nanoscience, bioscience, information technology, and cognitive science (NBIC) will have interlaced themselves within ongoing successful technologies, resulting in new and improved commercial endeavors. The impact of such eventualities would be enormous even if the emerging activities were developing independently, but with a range of synergies, their overlapping emergence and transitioning into the applied engineering arena promises to result in industrial products and technologies that stretch our imaginations to the point that they appear fanciful. Indeed, it is becoming more widely acknowledged that the potential of the new convergent NBIC technologies for influencing and defining the future is unlimited and likely unimaginable.

Nevertheless, leading personalities and recognized experts have attempted to gaze into the future as regards the character of the emerging technologies. What they herald are enterprises that dramatically impact mankind's physical environment, commerce, and, indeed, the performance of the human species itself. Intellectual leaders have divined some of the very likely near-term outcomes that will help determine the technologies that flourish beyond the 10-15-year timeframe. Examples of products of such technologies have ranged over the full panoply of futuristic outcomes, from unbelievably fast nanoprocessors to the creation of nanobots. Even more resolution to what we can anticipate is being provided in various forums associated with the present workshop focusing on NBIC technologies.

However, the emerging NBIC technologies — figuratively speaking, our starships into our future — will only take us as far as the skills of those who captain and chart the various courses. But acquisition of skills depends on many things, including most assuredly the existence of a positive social environment that allows creative juices to flow. As a result, educational issues, both *pedagogy* and *people,* surface as ingredients fundamental to the realization of successful technologies.

Pedagogy

It seems clear that progress in the NBIC arena will necessitate contributions from several fields whose practitioners have tended to address problems in a sequential manner. The operative approach has been, first something useful is found, then, if providence allows it, someone else gets involved with new insights or new capabilities; ultimately, commercial products are realized. In this era of convergent technologies, such a recipe can no longer be accepted, and practitioners must be taught in a new way.

This new pedagogy involves multidisciplinary training at the intersection of traditional fields, and it involves scientists, engineers, and social scientists. Although we still will need the ivory tower thinker, we will especially need to engage the intellects of students and established researchers in multidisciplinary, multi-investigator pursuits that lead to different ways of looking at research findings as well as to the utilization of different research tools. In acknowledgement of the necessity for multidiscipline skills and the participation in cross-discipline collaborations, nearly all of the funding agencies and private foundations provide substantial funding for research as well as for education of students in projects that are multidisciplinary and cross-disciplinary in character. A case in point is the Integrative Graduate Education and Research Training (IGERT) project (established by NSF in 1999), housed at The City University of New York, which involves three colleges from CUNY (the City College, Hunter College, and the College of Staten Island); Columbia University; and the University of Rochester.

IGERT participants are dedicated to the creation of research initiatives that span disciplinary and institutional boundaries, and to the objective that such initiatives be reflected in the education and training of all its students. The overall goal is to educate and train the next generation of scientists in an interdisciplinary environment whereby a graduate student may participate in all the phases of a research project: synthesis, materials fabrication, and characterization. Our students, though trained in as described, will be rigorously educated in a field of chemistry, engineering, or materials science. It is expected that such students will develop imaginative problem-solving skills and acquire a broad range of expertise and fresh, interdisciplinary outlooks to use in their subsequent positions. Our students will be not just sources of samples or instrument technicians but full partners with multidisciplinary training.

Without dealing with the specific science focus, the value-added elements of the CUNY-IGERT are described below:

- Multidisciplinary training (with choice of home institution after initial matriculation period at CUNY)
- IGERT focused seminar program (via video-teleconferencing)
- Reciprocal attendance of annual symposia
- Expanded training opportunities (rotations and extended visits to appropriate collaborating laboratories)
- Formalized special courses (utilizing distance learning technology)
- Credit-bearing enrichment activities and courses
- Collaborative involvement with industry and national laboratories
- International partnerships that provide a global perspective in the research and educational exposures of students

Such a model for coupling research and education will produce individuals capable of creatively participating in the NBIC arena.

The People

The second key educational issue concerns the people who make the science and engineering advances that will form the bedrock of new technologies. If these individuals are not equitably drawn from the populace at large, then one can predict with certitude that social equity and displacement issues will gain momentum with every advance, and can, in fact, dissipate or forestall the anticipated benefits of any endeavor.

It is thus clearly in America's best interest to ensure equitable participation of all elements in the front-line decision-making circles, in particular, to include groups that are historically underrepresented in leading-edge science and engineering, during this era of anticipated, unbridled growth of NBIC technologies. The rich opportunities to make contributions will help members of underrepresented groups, especially, to reassert and revalidate their forgotten and sometimes ignored historical science and technological prowess. Success here would go a long way to avoiding an enormous challenge to a bright future. What we stand to gain is the inclusion of the psychology and intellectual talents of an important segment of our society in solutions of ongoing and future world-shaping events. Two important activities immediately come to mind that make the point. One represents an opportunity lost, the second, a challenge we dare not ignore.

The first was NASA's space-venturing time capsule to other worlds several decades ago. Among many good things associated with this undertaking was one I consider unfortunate, a single-race representation of the inhabitants of the Earth. Clearly, a different psychological view, one more inclusive, should have prevailed, and probably would have if minorities had had a say.

The second is the mapping of the human genome. The resultant data bank, I should think, will reflect the proclivities and prejudices of its creators, and its exploitation in the battle against genetic diseases. Clearly we should all have a hand in what it looks like and how it is to be used.

Summary

Only by utilizing new educational approaches for providing NBIC practitioners with the skills and insights requisite for success and also by making sure that historically underrepresented citizens are not left behind can the full promise of this era of convergence be realized.

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CONVERGING TECHNOLOGY AND EDUCATION FOR IMPROVING HUMAN PERFORMANCE

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This statement will address two general issues. One relates to potential uses for nanotechnology in neuroscience and biomedical engineering. The other addresses suggested issues in the education of potential scientists who will be most effective in the development of the new technologies.

Potential Uses for Nanotechnology in Neuroscience Research and Biomedical Engineering

The following areas have the highest potential for application:

a) *Basic Neuroscience*

- Exploration of single neurons (see Zygmond et al. 1999, a graduate-level reference for the concepts presented below):
  - Develop nanoscale delivery systems for compounds relevant to the nervous system such as neurotransmitters or receptor blockers, etc. These would be used for distributed application to single cells in culture and *in situ*.
  - Develop nanoscale sensors, conductive fibers for stimulating and recording the electrical activity from the surface of single neurons.

- Combine delivery and sensing nanofibers with exploration of single neurons in culture, both soma and dendrites, both spread over surface of neuron

b) Observation and Study of Growing Cells

- Use sensors and delivery systems to study neuronal development or regenerating fibers *in situ.* This requires that nanosensors and nano-optical devices be placed in a developing or injured nervous system, either alone or in combination with MEMS or aVLSI devices

c) Development

- Monitor growth cones with nano-optical devices
- Provide growth factors with nanoscale delivery systems

d) Regeneration

- Study processes as neurons are attempting or failing to regenerate. How do neurons behave as they try to grow? What happens as they encounter obstacles or receptors?

e) Applications in Biomedical Engineering

The following applications assume that nanofibers can be grown or extruded from the tips of microwires *in situ:*

- Monitor spinal cord injury or brain injury
  - use nanofibers to assess the local levels of calcium in injury sites
  - use nano delivery systems to provide local steroids to prevent further damage
- Neuroprosthetic devices
  - Use nanofibers in conjunction with MEMS or aVLSI devices as delivery systems and stimulating devices for neuroprosthetic devices — make them more efficient.
  - Use CPG prosthetic device in conjunction with microwires to stimulate locomotion
  - Develop artificial cochlea with more outputs
  - Develop artificial retina with more complex sensors – in combination with aVLSI retinas

Figure F.2 illustrates the positioning of a cochlear implant in the human cochlea (Zygmond et al. 1999). These devices are in current use. The electrode array is inserted through the round window of the cochlea into the fluid-filled space called *scala tympani*. It likely stimulates the peripheral axons of the primary auditory neurons, which carry messages via the auditory nerve into the brain. It is presently known that the information encoded by the sparsely distributed electrodes is nowhere near that carried by the human cochlea. The device, therefore, is of limited value for hearing-impaired individuals with long-term auditory nerve damage that predates their normal speech learning (Moller 2001). If nanofibers could be deployed from each electrode to better distribute the information, it would likely improve the quality of the device considerably. This would be a relative easy use of the new technology, with easy testing to affirm its usefulness.

Training the Future Developers of Nanotechnology

In the new era of converging technologies, one can become either a generalist and be superficially capable in many fields, or one can become a specialist and master a single field. If one chooses the former route, one is unlikely to produce deep, insightful work. If one chooses the latter route, then it is only possible to take full advantage of the convergence of the technologies by working in collaboration with others who are expert in the other relevant fields. Unfortunately, our present educational system does not foster the type of individual who works well in collaborations.

To achieve the training of good scientists who have the capacity to work well in multidisciplinary groups, there are several new kinds of traits necessary. The first and perhaps most difficult is to learn to communicate across the disciplines. We learn the technical language of our respective disciplines and use it to convey our thoughts as clearly and precisely as possible. However, researchers in other disciplines are unfamiliar with the most technical language we prefer to use. When talking across the bridges we seek to build, we must learn to translate accurately but clearly to intelligent listeners who will not know our respective languages. We must begin to train our students to learn the skill of communicating across the disciplinary divides. We must develop programs in which students are systematically called upon to explain their work or the work of others to their peers in other areas. Thus, the best programs will be those that throw the students of the diverse disciplines together. Narrowly focused programs may turn out neuroscientists superbly trained for some functions, but they will not be good at collaborative efforts with scientists in other fields without considerable additional work. They will not easily produce the next generation of researcher who successfully forms collaborative efforts to use the new converging technologies.

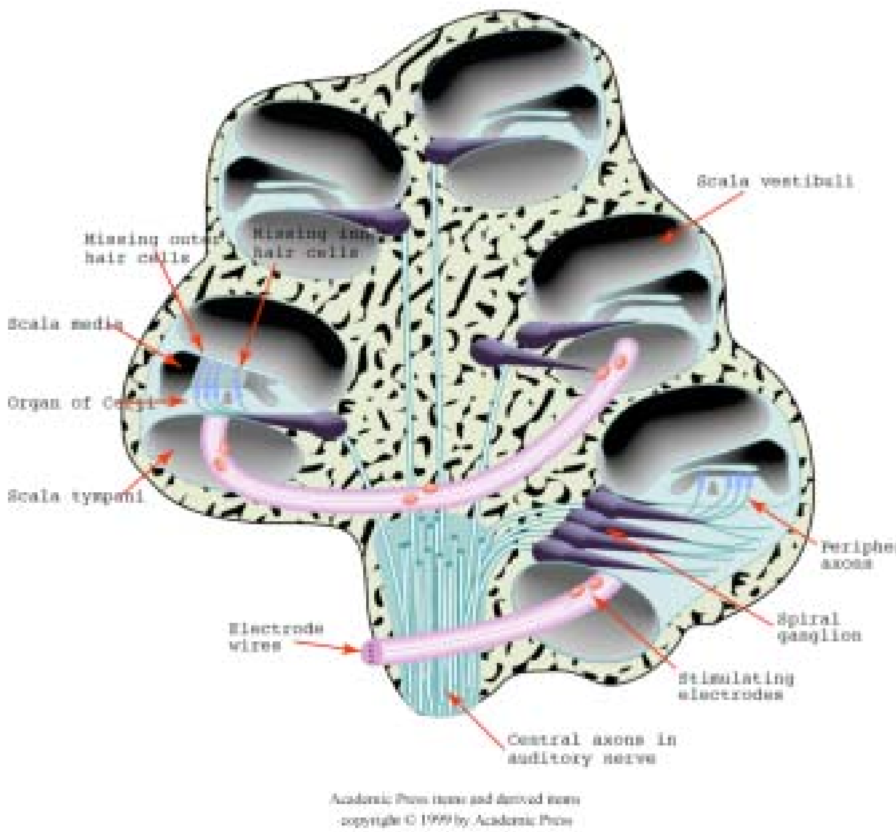

Figure F.2. The positioning of a cochlear implant in the human cochlea.

We should also begin to systematically pose challenges to our students such that they must work in teams of mixed skills, teams of engineers, mathematicians, biologists, chemists, and cognitive scientists. This will provide the flavor of the span that will be required. We cannot train our students to be expert in this broad a range of fields; therefore, we must train and encourage them to communicate across the range and to seek out and work with experts who offer the expertise that will allow the best science to be done. Funding agencies must continue to enlarge the mechanisms that support this type of work if they want to have a unique position in fostering the development and optimal utilization of the new technologies as applied to neuroscience, among other fields.

My experience with the Telluride Workshop on Neuromorphic Engineering has given me some important insights into the optimal methods for educating for the future. It has shown me that it will be easier to train engineers to understand biology, than to train biologists to comprehend engineering. There are some notable exceptions, fortunately, such as Miguel Nicolelis and Rodolfo Llinas. Among biologists, there is beginning to be curiosity and enthusiasm for engineering, robotics, and the new emerging technologies. This must be fostered through showcasing technological accomplishments such as successful robotic efforts and the analog VLSI retinas and cochleas developed using neuromorphic engineering. We must also try harder to get biologists to attend the Telluride Workshop and to stay long enough to gain some insights into the power of the approach. The field of nanobiotechnology is growing much faster among engineers than among biologists. We must work harder to improve our outreach to biologists.

The formation of workshops such as Telluride is a good venue for beginning to put together the necessary groups for the exploitation of the new methods being developed in nanotechnology. It is likely that the full potential for nanodevices will only be reached by uniting engineers with biologists. Biologists presently have little exposure to information about nanotechnology. Comparatively, the engineers know relatively little about the real neuronal substrate with which they seek to interface. It will not be a trivial task to actually understand what will emerge when nanotubes are directly contacting neurons, stimulating them, and recording from them. It will require considerable expertise and imagination. Exposing biologists to the potential power and usefulness of the technology, and exposing engineers to the complexity of the biological substrate, can only come about through intense interactions; it cannot come about through groups operating alone. The journal *Science* has done a great deal to bring nanotechnology to the attention of the general scientist. However, no true understanding can come without hard work.

Development of novel bioengineering programs will be another approach to development of nanotechnology. Training biologists and engineers in the same educational program will go a long way to overcoming some of the present ignorance. Nanotechnology is difficult. The underlying chemistry and physics will not come easily to everyone. It is most likely that the best method of developing it is through explicit programmatic efforts to build collaborative teams of engineers and biologists. Summer workshops can provide the incentives by exposing individuals to the potentials of the union, but only through full-fledged educational programs can the efforts move forward effectively.

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VISIONARY PROJECTS

CONVERGING TECHNOLOGIES: A K-12 EDUCATION VISION

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Over the next 15 years, converging technologies (CT), the synergistic interplay of nano-, bio-, information, and cognitive technologies (NBIC) will enable significant improvements in how, where, and what is taught in grades K-12 and will also support the lifelong learning required by a rapidly developing technological economy. Through national and state standards, half the schools in the United States will be teaching science based on the unifying principles of science and technology (NRC 1995) rather than the isolated subjects taught since before the industrial revolution. New tools for learning such as neuroscience sensors, increased quality of Internet service via guaranteed bandwidth, and a new understanding of biological feedback for self-improvement will provide new, highly efficient learning methods for all, in particular guaranteeing that all children can read by age five. Students will no longer be dependent on rigid regimentation of the classroom or schoolhouse and class schedule, as they will have courses and supplemental information available to them from numerous venues around the clock. Consider the following scenario.

The year is 2015. You enter a public school. From the outside, it appears to be much the same physical structure as schools were for 50 years. But inside is a totally different world. Teachers are busily meeting with one another and engaged in e-learning to stay current on the latest developments in education and their disciplines. They are contributing their experiences to a databank that parses the data into information and places it on an information website for other teachers and researchers to use. Science teachers are working in a cross-disciplinary program that has been particularly fruitful — NBIC — a wonderful stew of nanotechnology, biotechnology, information technology, and cognitive technologies. NBIC has allowed these teachers to productively access and continually learn new information through advances in small biological and neurological sensors and the biofeedback they produce. A number of special needs students are working in rooms, receiving cues from a wireless network that are appropriate for their individual cognitive and physical needs as developed through NBIC. Advances in NBIC research allow for better meeting the requirements of more and more special needs students each year with fewer human resources. Each student in the community can interact with other students worldwide to share information, language, and culture. While the student population of more than 50 million students has been joined by millions of parents as lifelong learning requirements are realized, no new buildings have been required, as many students take advantage of 24/7 availability of coursework at their homes, work areas, and at the school. The capital investment savings have been redirected into increased pay to attract and retain the highest quality teachers and curriculum developers. The line between education and recreation has blurred as all citizens visit the school building throughout the day to better their lives.

The Critical Roles of Converging Technologies

Converging technologies hold true promise to revolutionize the teaching in grades K-12 and beyond. The interplay of these technologies, each with the other, provides the opportunity for extraordinary advances in K-12 education on three fronts: content, process, and tools

Content

The recent extraordinary and rapid results of the Human Genome Project (HGP) provide for a revolution in the content of biology curriculum for K-12. The rapid completion of this project was due in a large part to the availability of IT-supported and -inspired experimental, analytical, and observational capability. While known as a "biology" project, the revolutionary advances are truly due to cross-disciplinary fertilization. CT offers K-12 education a focus that builds on the HGP accomplishments and provides content that folds in nanotechnology to understand the interactions of and to physically manipulate particles and entities at the fundamental sizes of the building blocks of life. New course content must be created that is sensitive to these developments and can be updated on an annual basis to be relevant to students' needs and the rapidly growing state of knowledge in the research fields. New courses that delve into the aspects of intelligent, sentient life and cognitive processes must also be developed. These courses must be created in the context of state-of-the-art and state-of-the-practice biotechnology, information technology, and nanotechnology. The state of Texas has already altered its formerly strictly discipline-structured curriculum with the insertion of an Integrated Physics and Chemistry Course. The content advances called for in this essay are in the same vein as the Texas advance but a quantum jump into the future – a jump necessary to serve students of the United States in a globally competitive economy (NAP 1995).

Process

A fundamental understanding of the physical or biological basis for cognition developed in CT will allow for a revolution in the individualization of the K-12 educational process. Psychologists currently study people's responses to stimuli and their ability to control their responses given certain physical data from their bodies (popularly known as biofeedback). However, to map the various learning modalities of children, physical and biological characteristics must be associated with a child's cognitive behaviors in such a way that genotypic or phenotypic mitigations can be identified and applied. The analysis of such data will require nano-, cogno-, bio-, and information technologies that are years beyond today's capabilities, as will the presentation of educational media once the appropriate intervention or course of treatment is identified.

Technologies for measuring brain activity and assessing cognitive function, representing advances in usability and sensitivity over the current electro-, magneto- and hemo-encephalographic technologies, will be developed that have the capability to go beyond diagnosing disorders to assessing students' learning strengths and weaknesses. This enhanced sensitivity will be enabled by advanced biotechnologies that are tuned to monitor cognitive function and will support the selection of appropriate remediation. Neurologically-based technologies will be available to assist in the remediation of learning impairments as well as to enhance the cognitive abilities of children. These technologies will extend a student's ability to concentrate and focus, to remember and retain, and to deal with stress.

Attention and memory enhancement technologies will be built upon computer-based cognitive rehabilitation technologies that are already available, as indicated in an NIH Consensus Statement (1998): "Cognitive exercises, including computer-assisted strategies, have been used to improve specific neuropsychological processes, predominantly attention, memory, and executive skills. Both randomized controlled studies and case reports have documented the success of these interventions using intermediate outcome measures. Certain studies using global outcome measures also support the use of computer-assisted exercises in cognitive rehabilitation."

Other education-related technologies include improvement of a student's attention and stress management abilities using brainwave and autonomic nervous system (ANS) biofeedback technologies. The Association for Applied Psychophysiology and Biofeedback (AAPB) has initiated a program "to assist educational and health professionals to teach children and youth to regulate their own bodies, emotions, relationships, and lives" (AAPB 2001).

Foreshadowing and early beginnings of this trend can already be seen, and it will gather momentum rapidly in the next few years. Computer software that simultaneously trains cognitive abilities directly relevant to academic performance and delivers brainwave biofeedback is used in school settings and is commercially available (Freer 2001). Biofeedback enrichment of popular video games (Palsson et al. 2001) has already been demonstrated to work as well as traditional clinical neurofeedback for attention deficit disorder. This same technology is also designed to deliver autonomic self-regulation training for stress management. Instrument functionality feedback, developed at NASA Langley Research Center, is a novel training concept for reducing pilot error during demanding or unexpected events in the cockpit by teaching pilots self-regulation of excessive autonomic nervous system reactivity during simulated flight tasks (Palsson and Pope 1999). This training method can also teach stressed youngsters to practice autonomic physiological self-regulation while playing video games without the need for conscious attention to such practice.

Embedding physiological feedback training into people's primary daily activities, whether work or play, is a largely untapped and rich opportunity to foster health and growth. It may soon be regarded to be as natural and expected as is the addition of vitamins to popular breakfast cereals. Toymakers of the future might get unfavorable reviews if they offer computer games that only provide "empty entertainment."

Twenty years from now, physiological feedback will be embedded in most common work tasks of adults and will be integral to the school learning and play of children. Interactions with computers or computer-controlled objects will be the predominant daily activity of both adults and children, and physiological feedback will be embedded in these activities to optimize functioning and to maintain well-being and health.

Tools

CT brings distance learning of today to a true 24/7 educational resource. Telepresence and intelligent agents will allow students to investigate fundamental biological questions through online laboratories and high-fidelity simulations. The simulations will be extensions of today's state-of-the-art distance surgery and robotic surgery. Actual data and its expected variations in physical attributes such as color, density, location, and tactile tension will be available in real time. Students in cities, suburbs, and remote rural areas will all have access to the same state-of-the-art content and delivery. These tools will first be available at central locations such as schools or libraries. As hardware cost and guaranteed available bandwidth allows, each home will become a school unto itself — providing lifelong learning for children and adult family members.

Delivery of learning experiences will be designed to enhance student attention and mental engagement. This goal will be supported in the classroom and at home by digital game-based learning (DGBL) experiences that provide (1) meaningful game context, (2) effective interactive learning processes including feedback from failure, and (3) the seamless integration of context and learning (Prensky 2001). Entertaining interactive lessons are available (Lightspan Adventures™) that run on a PC or a PlayStation® game console so that they can be used both in school and after school and in students' homes.

Patented technologies are also available that "use the latest brain research to develop a wide range of early learning, language and reading skills: from letter identification and rhyming to vocabulary and story analysis" for "children who struggle with basic language skills or attention problems" (Scientific Learning 2001).

Another set of educational tools enabled by CT, physiological monitoring, will be used to guide complex cognitive tasks. The recent proposal for NASA's Intelligent Synthesis Environment (ISE) project included an animation of a computer-aided design system responding to a user's satisfaction about a design iteration, measured via remote sensing of brainwaves. Similarly, a student's engagement in and grasp of educational material will be monitored by brain activity measurement technology, and the presentation can be adjusted to provide challenge without frustration.

Virtual reality technologies, another tool set, will provide the opportunity for immersive, experiential learning in subjects such as history and geography. Coupled with interactive simulations, VR environments will expand the opportunities for experiences such as tending of ecosystems and exploring careers. A NASA invention called "VISCEREAL" uses skin-surface pulse and temperature measurements to create a computer-generated VR image of what is actually happening to blood vessels under the skin (Severance and Pope 1999). Just as pilots use artificial vision to "see" into bad weather, students can use virtual reality to see beneath their skin. Health education experiences will incorporate realtime physiological monitoring integrated with VR to enable students to observe the functioning of their own bodies.

Transforming Strategy

The major technical barrier for instituting CT into the K-12 curriculum is the political complexity of the curriculum development process. Curriculum is the result of the influence of a number communities, both internal and external to the school district, as shown in Figure F.3.

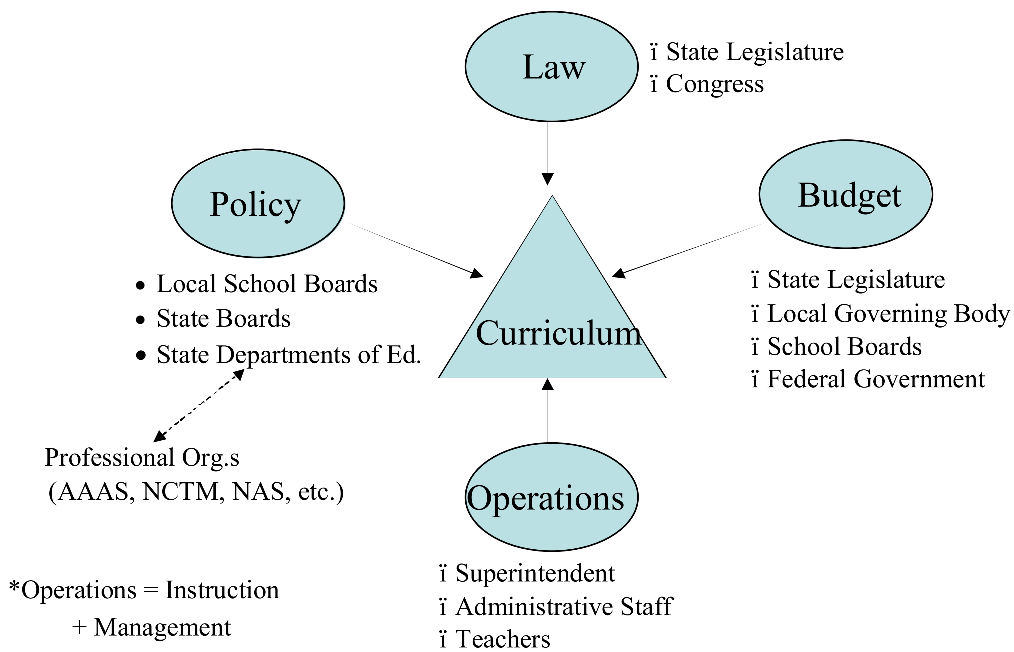

Figure F.3. The curriculum communities.

The CT Initiative must identify and work with all the appropriate K-12 communities to successfully create and integrate new curriculum — perhaps addressing a K-16 continuum. While teacher institutes occasionally can be useful, participatory partnering in real curriculum development promises to leave a lasting mark on more students and faculty. It is key to successful curriculum development to put together a coalition of teachers, administrators, students, parents, local citizens, universities, and industry for curriculum development. The virtual lack of any interdepartmental or cross-discipline courses in K-12 curricula is indicative of the gap that must be bridged to teach CT.

From the CT Initiative, courses can be created, but for *curriculum development*, the courses must be institutionalized or put into the context of the other courses in the school district. This institutionalization requires the involvement and support of the entire range of communities shown in Figure F.3.

There are approximately 50 million K-12 students in 15,000 school districts in the United States, its territories, and the District of Columbia. Reaching these districts or students individually would be virtually impossible. Rather, a major strategy should be to take advantage of the leverage available through impacting the national science education standards and emerging state standards (Figure F.4). At the national level, development and inclusion of CT curriculum involves development of national CT standards as a part of the national science education standards developed by the National Resource Council (NRC 1995). CT scientists should work for a regular review of the current standards and be prepared to provide CT standards as members of the review and standards committees.

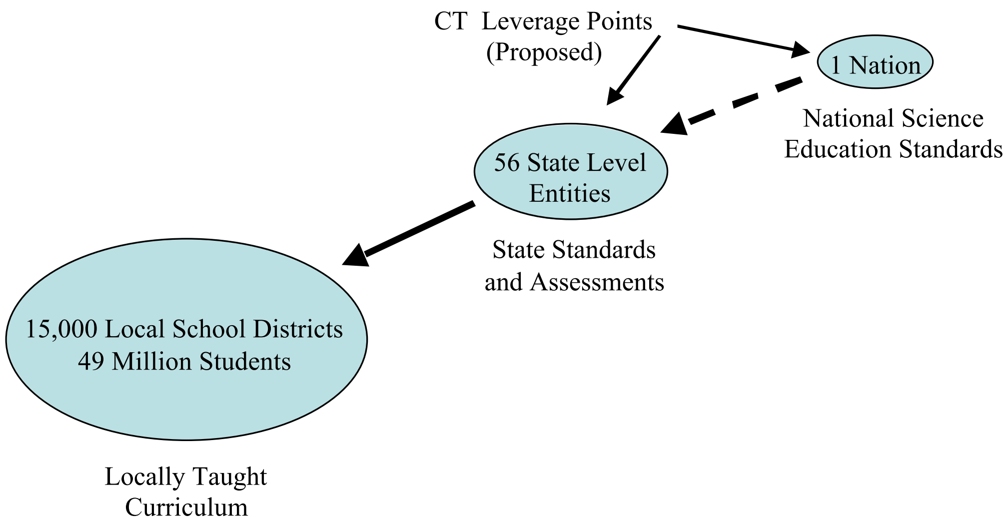

Figure F.4. Relationships between national and state standards and local school districts.

Because there is no U.S. national curriculum, having national CT standards serves only an advisory function. For these standards to be used in curriculum development, they need to be accepted by state boards of education in development of their separate state standards (Figure F.3 and Figure F.4). Each state must then have courses available that meet the standards it adopts. Many states have developed statewide assessments or tests for various subjects. A major step toward implementation of CT curricula would be positioning CT questions on statewide science assessment tests.

Complementary to the development of a K-12 curriculum *per se* is the development of a CT mentality in the general population and in the next generation of teachers and parents. Thus, development of CT courses at colleges in general, and in their teacher preparation departments in particular, is desirable.

Thus the transforming strategy for educational content has the following components:

- Influence over the National Science Education Standards (NRC)
- Development of CT science content standards
- Development of CT courses for K-12 to support the CT standards
- Influence on each state’s science standards and assessment instruments
- Development of CT courses for schools of education and in the general education of the next generation of university students

- Development, in cooperation with a writer of children's books, of "early reader" (ages 1-5) books containing CT concepts

Ethics

There will be ethical issues that arise regarding the ability to analyze each child's capacity to learn and develop. Categorization of humans relating to their abilities, and perhaps to their inferred potential in any area, may challenge many of our Western traditions and ethical values.

Implications

The implications of CT content, process, and tools for education of all children are dramatic. A specific focus would be the population of students today classified as "special education" students under IDEA (the Individuals with Disabilities Education Act – PL94-142). This includes approximately 10 percent of the entire age 3-17 cohort in the United States, or almost five and a half million children in the 6-21 year age bracket. More than one million of these children are diagnosed with speech or language impairment; 2.8 million with specific learning disabilities such as dyslexia; 600,000 with mental retardation; 50,000 with autism; and 450,000 with emotional disturbance.

In K-12 education, school district visions commonly aspire to educate all children to their full potential. The reality has been that many children are not educated to a level that allows them to be productive members of their adult society, let alone to their own full potential. While there is some differentiation of instruction and curriculum strands (such as special education, governor's schools, alternative education, and reading and hearing resource education), the ability to diagnose individual student needs is based on failure of a child to succeed in a "standard" early curriculum. It is only after such a failure that analysis begins with the possibility of a placement into one of several available alternative strands. These strands again treat a bulk condition identified empirically from phenotypic behaviors rather than treating an individual condition analyzed from the child's genotype. Individualization or fine-tuning of treatment is accomplished through labor-intensive one-on-one teaching. Our new vision, supported by convergent technologies, anticipates a future in which today's failures to successfully educate all children are mitigated through a fundamental physical understanding and modeling of cognitive and biological capabilities and processes in the young child. Appropriate mitigation and direction are based on early anticipation of the child's individual needs rather than bulk treatment after early failures.

The Glenn Commission (National Commission on Mathematics and Science Teaching for the 21st Century, Glenn 2000) estimated that the cost of meeting its three goals of improving science teaching quality with the current teachers, developing more science and math teachers, and improving the science and math teaching environment would cost approximately $5 billion in the first year. Roughly, this money would be used to provide teacher summer institutes, leadership training, incentives, scholarships, assessments, and coordination. Since this is aimed at all science and math teachers over a five-year program (there are 1.5 million science and math teachers for grades K-12 in the United States), CT could take early advantage of any implementation of a plan such as that proposed by the Glenn Commission.

Revisions in curriculum standards seem to take about five to ten years to develop, absent a major sea change in what is being taught. CT is a major change, and it further moves curriculum to stay current with scientific and technological advances. This will require regularly occurring curriculum reviews at the state level and the ability to adjust content and assessment with a factor of ten more efficiency than is done today. As a guide to the states, a national curriculum must also be reviewed and updated in a similarly regular way.

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EXPANDING THE TRADING ZONES FOR CONVERGENT TECHNOLOGIES

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Stimulating convergence among nano, bio, info and cognitive science obviously will require that different disciplines, organizations, and even cultures work together. To make certain this convergence is actually beneficial to society, still other stakeholders will have to be involved, including ethicists, social scientists, and groups affected by potential technologies. To promote this kind of interaction, we first need a vision — supplied, in this case, by a metaphor.

Vision: Developing "Trading Zones," a Metaphor for Working Together

A useful metaphor from the literature on science and technology studies is the trading zone. Peter Galison used it to describe how different communities in physics and engineering worked together to build complex particle detectors (Galison 1997). They had to develop a creole, or reduced common language, that allowed them to reach consensus on design changes:

> Two groups can agree on rules of exchange even if they ascribe utterly different significance to the objects being exchanged; they may even disagree on the meaning of the exchange process itself. Nonetheless, the trading partners can hammer out a *local* coordination, despite vast *global* differences. In an even more sophisticated way, cultures in interaction frequently establish contact languages, systems of discourse that can vary from the most function-specific jargons, through semispecific pidgins, to full-fledged creoles rich enough to support activities as complex as poetry and metalinguistic reflection (Galison 1997, 783).

My colleague Matt Mehalik and I have classified trading zones into three broad categories, on a continuum:

1. *A hierarchical trading zone governed by top-down mandates*. An extreme example is Stalinist agricultural and manufacturing schemes used in the Soviet Union (Graham 1993; Scott 1998) where the government told farmers and engineers exactly what to do. These schemes were both unethical and inefficient, stifling any kind of creativity. There are, of course, top-down mandates where the consequences for disobedience are less severe, but I would argue that as we look to the future of NBIC, we do not want research direction set by any agency or group, nor do we want a hierarchy of disciplines in which one dominates the others.

2. *An equitable trading zone state in which no one group is dominant*, and each has its own distinct perspective on a common problem. This kind of trading zone was represented by the NBIC conference where different people with expertise and backgrounds exchanged ideas and participated jointly in drafting plans for the future.

3. *A shared mental model trading zone based on mutual understanding of what must be accomplished*. Horizontal or lattice styles of business management are designed to promote this kind of state. An example is the group that created the Arpanet (Hughes 1998).

Another example is the multidisciplinary global group that invented a new kind of environmentally intelligent textile. Susan Lyons, a fashion designer in New York, wanted to make an environmental statement with a new line of furniture fabric. Albin Kaelin's textile mill in Switzerland was in an "innovate or die" situation. They started a trading zone around this environmental idea and invited the architect William McDonough, who supplied a mental model based on an analogy to nature, "waste equals food," meaning that the fabric had to fit smoothly back into the natural cycle in the same way as organic waste products. The architect brought in Michael Braungart, a chemical engineer who created and monitored detailed design protocols for producing the fabric. The actual manufacturing process involved bringing still others into the trading zone (Mehalik 2000).

Note that the shared mental model did not mean that the architect understood chemical engineering, or vice-versa. All members arrived at a common, high-level understanding of waste equals food, and translated that into their own disciplinary practices, while staying in constant touch with each other. The creoles that arise among Galison's communities are typically devoted to local coordination of practices. In this fabric case, we see a Creole-like phrase, "waste equals food," evolve into a shared understanding that kept different expertises converging on a new technology.

Role of Converging Technologies

Converging technologies designed to benefit society will involve trading zones with a shared mental model at the point of convergence. "Waste equals food" created a clear image of an environmental goal for the fabric network. Similar shared mental models will have to evolve among the NBIC areas.

The process of technological convergence will not only benefit from trading zones, it can play a major role in facilitating them. Consider how much easier it is to maintain a transglobal trading zone with the Internet, cell phones, and air transport. Imagine a future in which convergent technologies make it possible for people to co-locate in virtual space for knowledge exchange, with the full range of nonverbal cues and sensations available. Prototypes of new technological systems could be created rapidly in this virtual space and tested by representatives of stakeholders, who could actually make changes on the fly, creating new possibilities. The danger, of course, is that these virtual prototypes would simply become an advanced form of vaporware, creating an inequitable trading zone where technology is pushed on users who never have full information. But in that case, new trading zones for information would emerge, as they have now — witness the success of *Consumer Reports.* It is essential that powerful new technologies for disseminating and creating knowledge be widely accessible, not limited to an elite.

Transforming Strategies

Effective trading zones around convergent technologies cannot be created simply by bringing various groups together, although that is a first step. Here, federal agencies and foundations can form a trading zone around resources (see Fig. F.5) — like the role of the National Science Foundation in the National Nanotechnology Initiative. This kind of program must not micromanage the sort of research that must be done; instead, it has to provide incentives for real engagement among different cultures of expertise.

Technologies designed to improve human health, increase cognitive performance, and improve security will have to fit into global social systems. We need to create active technological and scientific trading zones built around social problems. These trading zones will require experts with depth in relevant domains. The trading zones will need to provide incentives for them to come together, including opportunities to obtain funding and to work on "sweet" technological problems (Pacey 1989). In addition, each zone will require a core group of practitioners from different disciplines to share a mental model of what ought to be accomplished.

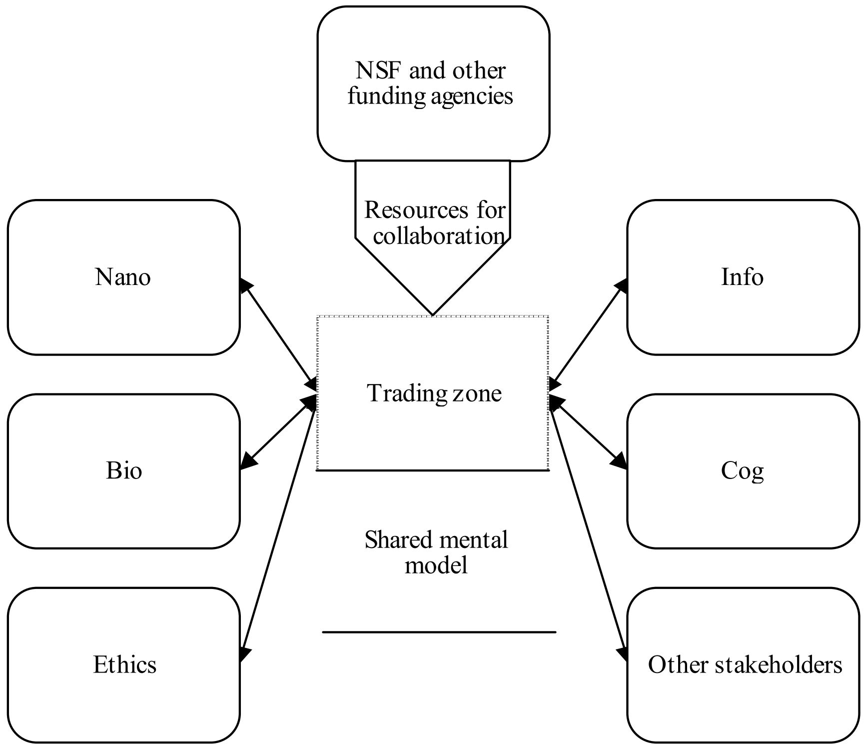

Figure F.5. Technologies converging on a trading zone seeded by resources that encourage collaboration.

Here, it is worth recalling that mental models are flexible and adaptable (Gorman 1992; Gorman 1998). One good heuristic for creating a flexible shared mental model came up repeatedly during the conference: "follow the analogy of nature." Alexander Graham Bell employed this heuristic in inventing the telephone (Gorman 1997). Similarly, McDonough's "waste equals food" mental model is based on the analogy to living systems, in which all organic waste is used as food by forms of life.

Similarly, as we look at beneficial ways in which human performance can be enhanced, it makes sense to study the processes and results of millions of years of evolution, which have affected not only biological systems, but also the climate cycles of the entire planet (Allenby 2001). The pace of technological evolution is now so fast that it exceeds the human capacity to reason about the consequences. Hence, we have to anticipate the consequences — to attempt to guide new discoveries and inventions in a beneficial direction. Nature's great inventions and failures can be a powerful source of lessons and goals. As Alan Kay said, "The best way to predict the future is to create it."

We see NASA adopting this analogy to nature when it proposes aircraft that function like high-technology birds, with shifting wing-shapes. The human ear served as Alexander Graham Bell's mental model for a telephone; in the same way, a bird might serve as a mental model for this new kind of aircraft. Creating this kind of air transport system will require an active trading zone among all of the NBIC areas, built around a shared mental model of what needs to be accomplished.

Good intellectual trading zones depend on mutual respect. Hard scientists and engineers will have to learn to respect the expertise of ethicists and social scientists, and vice-versa. The ethicist, for example, cannot dictate moral behavior to the scientists and engineers. Instead, she or he has to be ready to trade expertise, learning about the science and engineering while those practitioners get a better understanding of ethical issues.

Consider, for example, a trading zone between the medical system and its users around bioinformatics. Patients will be willing to trade personal information in exchange for more reliable diagnoses. But the patients will also have to feel they are being treated with respect — like human beings, not data points — or else the trading zone will break down.

In terms of education, what this means is that we want to encourage students to go deeply into problems, not necessarily into disciplines. Elementary students do not see the world divided into academic categories; instead, they see interesting questions. As they pursue these questions, they should be encouraged to engage deeply. But the result will be new kinds of expertise, not necessarily easily labeled as "physics," "chemistry," or "biology." The best trading zones are built around exciting problems by practitioners eager to create the knowledge necessary for solutions. And every such trading zone ought to include practitioners concerned about the social dimensions of technology.

Communications is the key to a successful trading zone. Students need to be given opportunities to work together in multidisciplinary teams, sharing, arguing, and solving difficult, open-ended problems together. Teachers need to scaffold communications in such teams, helping students learn how to present, write, and argue constructively. We have a long tradition of doing this in our Division of Technology, Culture, and Communication in the Engineering School at the University of Virginia (http://www.tcc.virginia.edu).

Estimated Implications

The great thing about trading zones is that successful ones expand, creating more opportunities for all of us to learn from each other. Hopefully, the first NBIC meeting has provided a foundation for such a trading zone between nano, bio, info, and cogno practitioners — and those in other communities like ethics, politics, and social relations.

We must remember to accompany the creation of convergent trading zones with detailed studies of their development. One of the most valuable outcomes would be a better understanding of how to encourage the formation of convergent, multidisciplinary trading zones.

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BIOLOGICAL LANGUAGE MODELING: CONVERGENCE OF COMPUTATIONAL LINGUISTICS AND BIOLOGICAL CHEMISTRY

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How can we improve the nation's productivity and quality of life in the next 10-20 years? The nation's performance is dependent on functions of the human body, since they directly or indirectly determine human ability to perform various tasks. There are two types of human ability: (1) "inherent abilities," tasks that humans are able to perform, and (2) "external abilities," tasks that we cannot perform *per se*, but for which we can design machines to perform them. Both categories have individually experienced groundbreaking advances during the last decade. Our inherent abilities in terms of fighting diseases, repair of malfunctioning organs through artificial implants, and increased longevity have greatly improved thanks to advances in the medical and life sciences. Similarly, technology has provided us with remarkable tools such as smaller and more efficient computers; the Internet; and safer, cleaner, and cheaper means of transport.

Integration of Inherent and External Human Abilities

Advancing our society further necessitates a better integration between the inherent and external abilities. For example, interfacing computers with humans need not require keyboard and mouse: ongoing efforts advance utilization of speech interfaces. But ultimately, it would be desirable to directly interface with the human brain and other organs. This will require further advances in elucidating the fundamental biological mechanisms through which humans think, memorize, sense, communicate, and act. Understanding these mechanisms will allow us to (a) modify our inherent abilities where natural evolution does not feel any pressure for improvement and (b) design interfaces that connect our inherent abilities with external abilities.

Grand Challenge: Mapping Genome Sequence Instructions to Inherent Abilities

How can we aim to understand complex biological systems at a level of detail sufficient to improve upon them and build interfaces to external machines? In principle, all the information to build complex biological systems is stored in an "instruction manual," an organism's (e.g., a human's) genome. While we have recently witnessed the elucidation of the entire human genome sequence, the next logical grand challenge for the coming decade is to map the genome sequence information to biological functions. Interfacing between biological functions and artificially manufactured devices will require improved structure-property understanding as well as manufacturability at a multiscale level ranging from Ångstrom-sized individual components of biological molecules to macroscopic responses. This will be possible through existing and future advances in nanotechnology, biological sciences, information technology and cognitive sciences (NBIC).

Outline

The sequence → function mapping question is conceptually similar to the mapping of words to meaning in linguistics (Figure F.6). This suggests an opportunity to converge two technologies to address this challenge: computational linguistics and biological chemistry, via "biological language modeling." The term "biological chemistry" is used here to stand for interdisciplinary studies of biological systems, including biochemistry, molecular biology, structural biology, biophysics, genetics, pharmacology, biomedicine, biotechnology, genomics, and proteomics. The specific convergence of linguistics and biological chemistry is described below under the heading, "The Role of Converging Technologies: Computational Linguistics and Biological Chemistry." Its relation to the more general convergence with NBIC is described in section, "The Role of Converging Technologies: NBIC and Biological Language Modeling." Two specific applications of linguistic analysis to biological sequences are given in "The Transforming Strategy," to demonstrate the transforming strategy by example. If we can solve the sequence → function mapping question, the implications for human performance and productivity are essentially unlimited. We have chosen a few practical examples to illustrate the scope of possibilities ("The Estimated Implications"). Implications for society are sketched in "Implications for Society," followed by a brief summary.

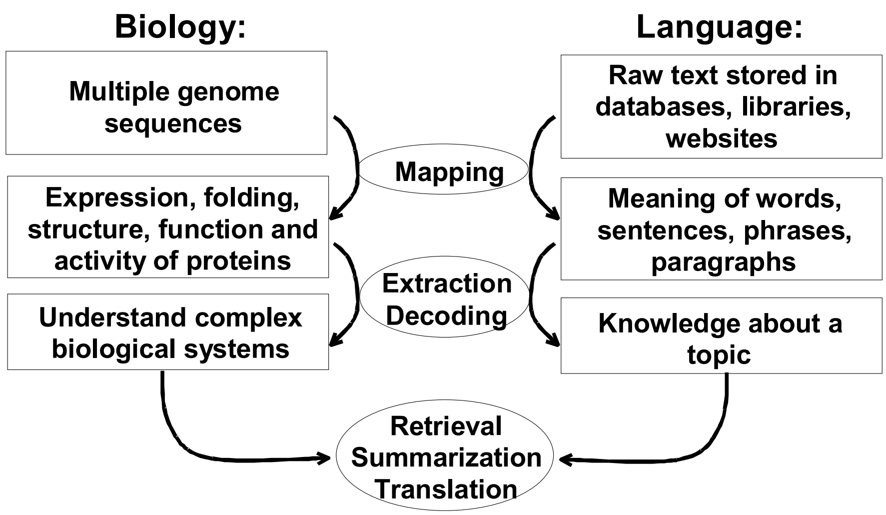

Figure F.6. Analogy between language and biology, which forms the basis for the convergence of computational linguistics and biological chemistry.

The Role of Converging Technologies: Computational Linguistics and Biological Chemistry

Complex biological systems are built from cells that have differentiated to perform specialized functions. This differentiation is achieved through a complicated network of interacting biological molecules. The main action is carried out by proteins, which are essentially nano-sized biological machines that are composed of string of characteristic sequences of the 20 amino acid building blocks. The sequences of the strings are encoded in their entirety in the genome. The linear strings of amino acids contain in principle all the information needed to fold a protein into a 3-D shape capable of exerting its designated function. With the advent of whole-genome sequencing projects, we now have complete lists of all the protein sequences that define the complex function carried out by the sequenced organisms — hundreds to thousands in bacteria and tens of thousands in humans. Individual proteins and functions have been studied for decades at various levels — atomic to macroscopic. Most recently, a new field has evolved, that of proteomics, which looks at all the proteins in a cell simultaneously. This multitude of data provides a tremendous new opportunity: the applicability of statistical methods to yield practical answers in terms of likelihood for biological phenomena to occur.

It is the availability of enormous amounts of data that has also transformed linguistics. In language, instead of genome sequences, raw text stored in databases, websites, and libraries maps to the meaning of words, phrases, sentences, and paragraphs as compared to protein structure and function (Figure F.6). After decoding, we can extract knowledge about a topic from the raw text. In language, extraordinary success in this process has been demonstrated by the ability to retrieve, summarize, and translate text. Examples include powerful speech recognition systems, fast web document search engines, and computer-generated sentences that are preferred by human evaluators in their grammatical accuracy and elegance over sentences that humans build naturally. The transformation of linguistics through data availability has allowed convergence of linguistics with computer science and information technology. Thus, even though a deep fundamental understanding of language is still missing, e.g., a gene for speech has only been discovered a few months ago (Lai et al. 2002), data availability has allowed us to obtain practical answers that fundamentally affect our lives. In direct analogy, transformation of biological chemistry by data availability opens the door to convergence with computer science and information technology. Furthermore, the deeper analogy between biology and language suggests that successful sequence → function mapping is fundamentally similar to the ability to retrieve, summarize, and translate in computational linguistics. Examples for biological equivalents of these abilities are described below under "The Estimated Implications."

The Role of Converging Technologies: NBIC and Biological Language Modeling

The strength of the analogy between biology and language lies in its ability to bridge across scales — atomic, nanostructural, microstructural, and macroscopic — enabling profit from the convergence of other disciplines (Figure F.7). Ideally, we would like to correlate complex biological systems, including their most complex abilities — the cognitive abilities of the brain, such as memory — with the individual atoms that create them. Rapid advances currently occur at all scales because of the convergence of technologies, allowing us to collect more data on natural systems than we were ever able to collect before. The data can be analyzed using information technology at all levels of the hierarchy in scale. Furthermore, mapping can involve any levels of the hierarchy, e.g., atomic → macroscopic or nanostructural → microstructural. The language analogy is useful here because of the hierarchical organization of language itself, as manifested by words, phrases, sentences, and paragraphs.

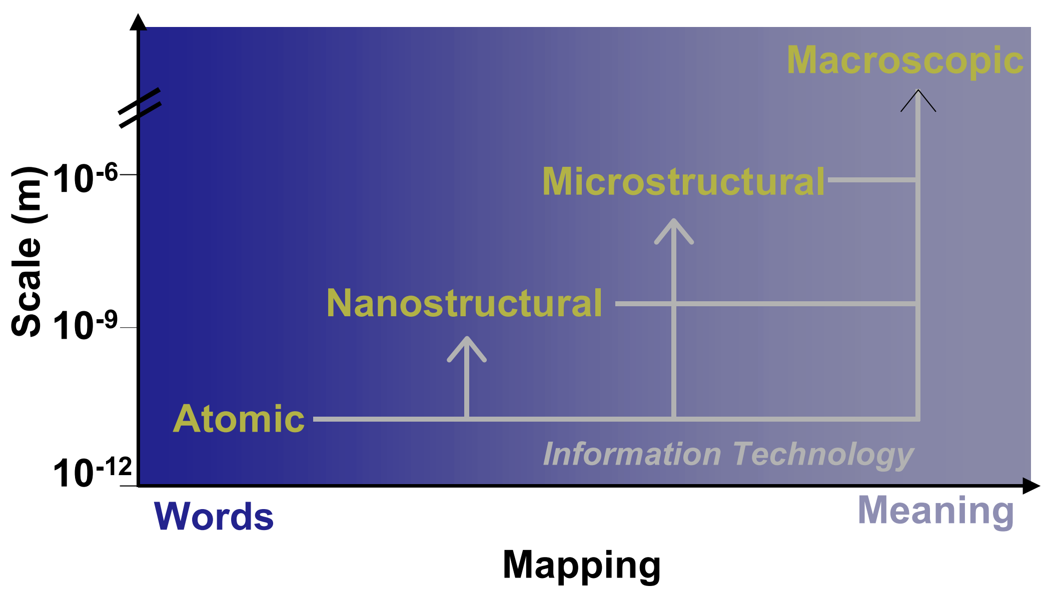

Figure F.7. Biological language modeling allows bridging across scales via the mapping of words to meaning using information technology methods, in particular computational linguistics.

The Transforming Strategy

One test for convergence of technologies is that their methods are interchangeable, i.e., language technologies should be directly applicable to biological sequences. To date, many computational methods that are used extensively in language modeling have proven successful as applied to biological sequences, including hidden Markov modeling, neural network, and other machine learning algorithms, demonstrating the utility of the methodology. The next step is to fully explore linguistically inspired analysis of biological sequences. Thus, the Carnegie Mellon and Cambridge Statistical Language Modeling (SLM) Toolkit, utilized for natural language modeling and speech recognition in more than 40 laboratories worldwide, was applied to protein sequences, in which the 20 amino acids were treated as words and each protein sequence in an organism as a sentence of a book. Two exemplary results are described here.

1. In human languages, frequent words usually do not reveal the content of a text (e.g., “I”, “and”, “the”). However, abnormalities in usage of frequent words in a particular text as compared to others can be a signature of that text. For example, in Mark Twain’s “Tom Sawyer”, the word “Tom” is amongst the top 10 most frequently used words. When the SLM toolkit was applied to protein sequences of 44 different organisms (bacterial, archaeal, human), specific n-grams were found to be very frequent in one organism, while the same n-gram was rare or absent in all the other organisms. This suggests that there are organism-specific phrases that can serve as “genome signatures.”

2. In human languages, rare events reveal the content of a text. Analysis of the distribution of rare and frequent n-grams over a particular protein sequence, that of lysozyme, a model system for protein folding studies, showed that the location of rare n-grams correlates with nucleation sites for protein folding that have been identified experimentally (Klein-Seetharaman 2002). This striking observation suggests that rare events in biological sequences have similar status for the folding of proteins, as have rare words for the topic of a text.

These two examples describing the usage of rare and frequent “words” and “phrases” in biology and in language clearly demonstrates that convergence of computational linguistics and biological chemistry yields important information about the mapping between sequence and biological function. This was observed even when the simplest of computational methods was used, statistical n-gram analysis. In the following, examples for the potential benefits of such information for improving human health and performance will be described.

The Estimated Implications

Implications for Fundamental Understanding of Properties of Proteins

The convergence of linguistics and biology provides a framework to connect biological information gathered in massive numbers of studies, including both large-scale genome-wide experiments and more traditional small-scale experiments. The ultimate goal is to catalogue all the words and their respective meanings occurring in genomic sequences in a “biological dictionary.” Sophisticated statistical language models will be able to calculate the probabilities for a specific amino acid within a protein context. It will be possible to examine what combinations of amino acid sequences give a meaningful sentence, and we will be able to predict where spelling mistakes are inconsequential for function and where they will cause dysfunction.

Cataloguing Biological Languages at Hierarchical Levels: Individual Proteins, Cell Types, Organs, and Related and Divergent Species

The language modeling approach is applicable to distinguishing biological systems at various levels, just as language varies among individuals, groups of individuals, and nations. At the most fundamental level, we aim at deciphering the rules for a general biological language, i.e., discovering what aspects are common to all sequences. This will enhance our fundamental understanding of biological molecules, in particular how proteins fold and function. At the second level, we ask how differences in concentrations, interactions, and activities of proteins result in formation and function of different cell-types and ultimately of organs within the same individual. This will allow us to understand the principles underlying cell differentiation. The third level will be to analyze the variations among individuals of the same species, the single nucleotide polymorphisms. We can then understand how differences in characteristics, such as intelligence or predisposition for diseases, are encoded in the genome sequence. Finally, the most general level will be to analyze differences in the biological languages of different organisms, with varying degree of relatedness.

Ideally, all life on earth will be catalogued. The impact on understanding complexity and evolution of species would be profound. Currently, it is estimated that there are 2-100 million species on earth. While it is not feasible to sequence the genomes of all the species, language modeling may significantly speed up obtaining "practical" sequences (Figure F.8). One of the bottlenecks in genome sequencing is the step from draft to finished sequence because of error correction and filling of gaps. However, if we define a vocabulary of the words for an organism from a partial or draft sequence, we should be able to predict blanks and correct mistakes in forward and backward direction using language modeling.

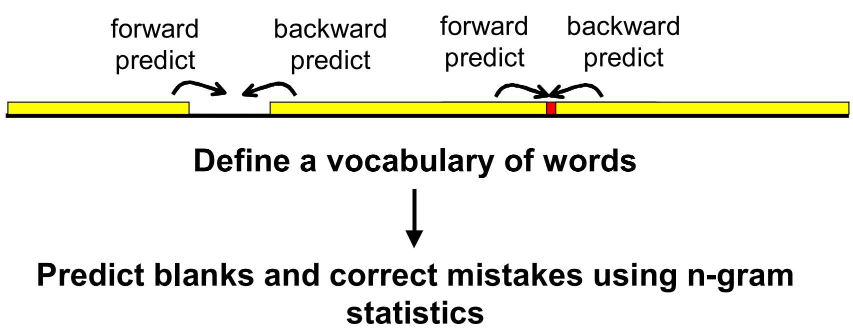

Figure F.8. Opportunity for biological language modeling in genome sequences.

Retrieval, Summarization, and Translation of Biological Sequences

As in human language modeling, success in biological language modeling will be measured by the capacity for efficient (1) retrieval, (2) summarization, and (3) translation:

1. When we desire to enhance the performance of a specific human ability, we can *retrieve* all the relevant biological information required from the vast and complex data available.

2. We can *summarize* which proteins of a pathway are important for the particular task, or which particular part of a key protein is important for its folding to functional 3-D structure. This will allow modifications of the sequences with the purpose of enhancing the original or adding a new function to it. Successful existing examples for this strategy include tagging proteins for purification or identification purposes.

3. Finally, we can *translate* protein sequences from the "language" of one organism into that of another organism. This has very important implications, both for basic sciences and for the biotechnology industry. Both extensively utilize other organisms, i.e., the bacterium *E. coli*, to produce human proteins. However, often proteins cannot be successfully produced in *E. coli* (especially the most interesting ones): they misfold, because the environment in bacterial cells is different from that in human cells (Figure F.9). Statistical analysis of the genomes of human and *E. coli* can demonstrate the differences in rules to be observed if productive folding is to occur. Thus, it should be possible to alter a human protein sequence in such a way that it can fold to its correct functional 3-D shape in *E. coli*. The validity of this hypothesis has been shown for some

examples where single point mutations have allowed expression and purification of proteins from *E. coli*. In addition to the traditional use of *E. coli* (or other organisms) as protein production factories, this translation approach could also be used to add functionality to particular organisms.

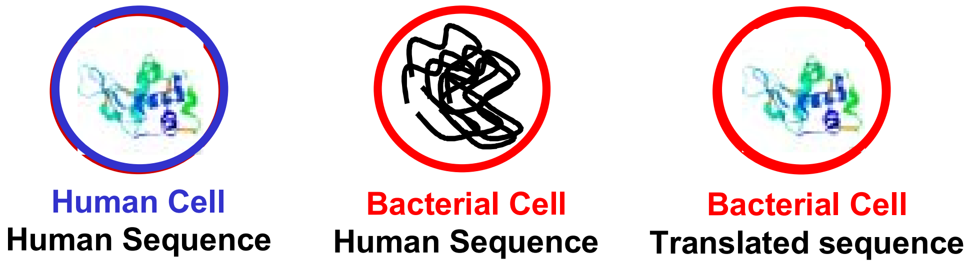

Figure F.9. Opportunity for biological language modeling to overcome biotechnological challenges. Misfolding of human proteins in bacterial expression systems is often a bottleneck.

Implications for Communication Interfaces

The ability to translate highlights one of the most fundamental aspects of language: a means for communication. Knowing the rules for the languages of different organisms at the cellular and molecular levels would also allow us to communicate at this level. This will fundamentally alter (1) human-human, (2) human-other organism, and (3) human-machine interfaces.

1. Human-human communication can be enhanced because the molecular biological language level is much more fundamental than speech, which may in the future be omitted in some cases as intermediary between humans. For example, pictures of memory events could be transmitted directly, without verbal description, through their underlying molecular mechanisms.

2. The differences in language between humans and other organisms can be exploited to "speak" to a pathogen in the presence of its human host (Figure F.10). That this may be possible is indicated by the observation of organism-specific phrases described in "The Transforming Strategy." This has important implications for the fight against bioterrorism and against pathogens in general to preserve and restore human health. The genome signatures should dramatically accelerate vaccine development by targeting pathogen-specific phrases. The advantage over traditional methods is that multiple proteins, unrelated in function, can be targeted simultaneously.

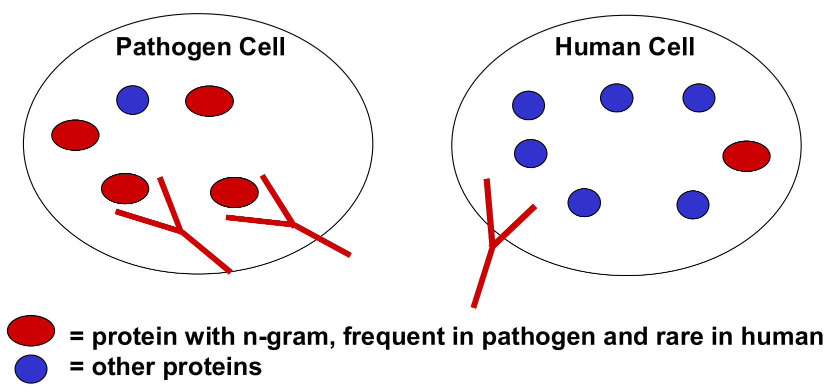

Figure F.10. Opportunity for biological language modeling to dramatically speed vaccine or drug development by simultaneously targeting multiple proteins via organism-specific phrases.

3. Finally, there are entirely novel opportunities to communicate between inherent and external abilities, i.e., human (or other living organisms) and machines. Using nanoscale principles, new materials and interfaces can be designed that are modeled after biological machines or that can interact with biological machines. Of particular importance are molecular receptors and signal transduction systems.

Implications to Rationalize Empirical Approaches

The greatest exploitation of the sequence → structure/function mapping by computational linguistics approaches will be to rationalize empirical observations. Here are two examples.

1. The first example concerns the effect of misfolding of proteins on human health. The correlation between the distribution of rare amino acid sequences in proteins and the location of nucleation sites for protein folding described above is important because misfolding is the cause of many diseases, including Alzheimer's, BSE, and others, either because of changes in the protein sequence or because of alternative structures taken by the same sequences. This can lead to amorphous aggregates or highly organized amyloid fibrils, both interfering with normal cell function. There are databases of mutations that list changes in amyloid formation propensity. Studying the linguistic properties of the sequences of amyloidogenic wild-type and mutant proteins may help rationalizing the mechanisms for misfolding diseases, the first step towards the design of strategies to treat them.

2. The second example is in tissue engineering applications (Figure F.11). The sequence → structure/function mapping also provides the opportunity to engineer functionality by rationalized directed sequence evolution. Diseased or aged body parts, or organs whose performance we might like to enhance, all need integration of external materials into the human body. One typical application is bone tissue engineering. The current method to improve growth of cells around artificial materials such as hydroxyapatite is by trial and error to change the function of co-polymers and of added growth factors. Mapping sequence to function will allow us to rationally design growth factor sequences that code for altered function in regulating tissue growth.

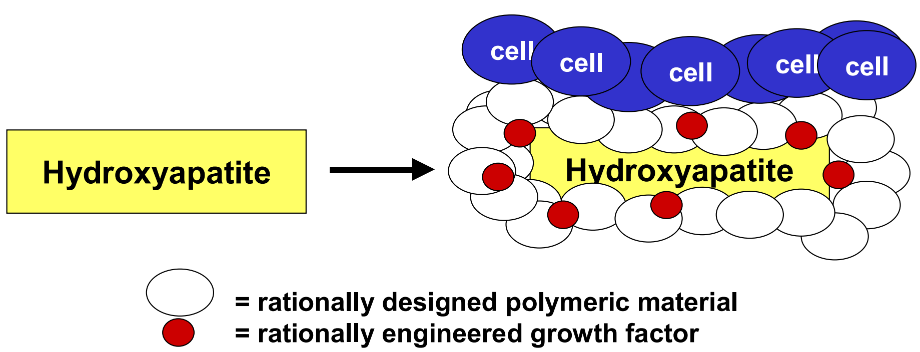

Figure F.11. Opportunity for biological language modeling to rationalize tissue engineering via engineering of growth factors and artificial materials.

Implications for Society

The above scenario has important implications for economic benefits, including cheaper and faster drug development, overcoming bottlenecks in biotechnology applications, cheaper and better materials and machines that perform old and new tasks, and environmental benefits. A key challenge will be to maintain reversibility in all changes that are made to living organisms to prevent unwanted environmental catastrophes, such as predominance of new organisms with enhanced capabilities in the environment. These new technologies require drastic changes in education. Human learning, memory, and creativity — which is likely to increase as a result of the revolutions in biology — have to be steered towards attaining literacy in health and biology for all citizens. Close collaboration between academic and industrial partners will allow universities to focus on fundamental advances keeping in mind the implications and potential applications that will be evaluated and realized by industry.

Summary

Human performance and the nation's productivity will increase drastically if existing and new biological knowledge is exploited by statistical methods to obtain practical answers to the fundamental questions:

- How can we enhance human inherent abilities?
- How can inherent and external abilities be better integrated?

The analogy between language and biology will provide a framework for addressing these questions through convergence of computational linguistics with biological chemistry within the broader context of NBIC. The challenge is to achieve successful mapping of genome sequence to structure and function of biological molecules. It would then be possible to integrate man-made machines into the human body with interfaces at the cellular and molecular level, for example, sensors for biological, chemical, or physical changes in the environment. Artificial organs will perform traditional functions better than youthful, healthy natural organs, or be able to perform new functions. By exploiting differences in languages between different organisms, novel strategies to fight pathogenic infections will emerge. New functions will be built into organisms that lack them. The maximum benefit will be possible if all knowledge is catalogued in a way that it can be accessed efficiently via computers today and in the future by nanomachines of all kinds. The biology-language analogy provides the means to do so if an encyclopedia for vocabulary and rules of biological language can be developed.

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Appendix C. Index of Topics

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