Parameters for a research mobilization against AIDS

A real war on AIDS will make use of the most advanced technologies, techniques, and ideas in biological science. Part two of Jonathan Tennenbaum's report.

This second installment of the article continues to review the instruments of optical biophysics, which began last week with the discussion of 1) Laser Raman spectroscopy and the "tuning" of living tissue, and 2) multiparameter light scattering. After examining the leading work on these technologies, we shall indicate how they provide to answering those questions about AIDS, which today's molecular biology is unable to resolve.

The instruments of optical biophysics

3. Ultraweak photon emission from living cells. The discovery of ultraweak light emission from living tissue and gradual unraveling of its biological significance, in work spanning from the Russian researcher A. Gurwitsch in the 1920s to the work of Fritz-Albert Popp and his group today, must be classed among the most far-reaching biological discoveries of this century.

All living cells spontaneously emit a weak light radiation at intensities of the order of 10-100 photons per second per square centimeter tissue surface, over a broad frequency range from infrared into the ultraviolet. Thanks to the perfection of photomultiplier tubes and, more recently, of sensitive solid state sensors, this radiation can be measured precisely. The instrument employed by Dr. F-A. Popp at his laboratory in Kaiserslautern, West Germany is sensitive enough to detect the light of a firefly at a distance of 5 kilometers!

The most immediate commercial application of this ultraweak photon emission (UPE) detection technology is in the measurement of potential toxic effects of various drugs. When even minute quantities of a toxic substance are introduced to a cell culture, we register a rapid "burst" of photon emission, indicating a disruption of the normal "least action" configuration of the living system. A "hybrid" biological-physical detector, Popp's system may constitute the most sensitive detector of various toxic substances in existence today—with potential applications in studies of pollution, in pharmacotoxology, forensic medicine, and defense.

Such practical applications are far outshadowed by the implications of UPE in fundamental research. Although the total amount of energy measured at the photon detector is very small, the *energy density* of the radiation *inside* the cell may be large. Relative to events on the "molecular" level, a single photon in the ultraviolet range is the equivalent of a heavy artillery shot: A single ultraviolet photon suffices to fracture a powerful chemical bond, activate an enzyme or send an electron through a long chain of transformations. Experiments by the Soviet spectroscopist Prokhorov show that a single ultraviolet photon suffices, under certain conditions, to trigger the division of a cell.

More important still is to understand why any disturbance to living tissue *increases* the light emission. This fact points to two main conclusions: 1) The source of the UPE is "universal" in the sense that it is affected by every change occurring in the tissue. In fact, as Popp has shown, the UPE has coherent, "laser-like" properties characteristic of a single, unified source rather than a mere collection of independent sources. Thus, the UPE of normal tissue derives from a coherent field "coupling" the activities of thousands of mil-

lions of cells via long-distance electromagnetic interactions. 2) In normal tissue, the actual photon flux is much higher than the residue measured outside. Undisturbed tissue tends toward least action states in which almost all emitted energy is coherently observed in the work processes of the cells. Disruption of a least action state results in the incoherent release of "unused" photons, which Gurwitsch called "degradation radiation."

Evidence assembled by Popp and others points to a central role of cell nucleus DNA in the observed photon emission. This may finally explain an anomaly which has much embarrassed the molecular biologists: More than 95% of the DNA in human, animal, and plant cells has no "coding" function in the production of proteins. Rather than accept the fact that living cells do not function in the digital computer-like fashion some would like to imagine, dogmatic molecular biologists like Crick insist on slandering this 95% of the genetic material as "parasitical" or "junk" DNA! More likely, it is the dogmas of molecular biology which are the "junk." Popp has a much better hypothesis: Experiments and calculations show that the DNA molecule can function as an ideal *microscopic laser*, storing energy in a ratchet-like process and releasing it again in coherent bursts at shorter wavelengths. In this process, the nucleotide pairs form exciplexes—metastable excited complexes similar to the excimers employed in short-wavelength laser technology (excimer lasers). The pumping energy for this process derives from the cell metabolism. Living tissue produces 10^{40} times more ultraviolet radiation than nonliving matter at the same temperature. As opposed to most technical lasers, which work only at one or a few wavelengths, the DNA functions as a *multimode* laser, putting out perhaps thousands of different frequencies and regulating, via the resonant absorption of specific frequencies by specific cell processes, the entire complex of metabolic activity in the tissue. These, at least, are the working hypotheses around which Popp et al. are gathering a remarkable complex of theoretical and experimental work.

The fruitfulness of Popp's approach has already been demonstrated in cancer research, an area very close to that of AIDS. The emission characteristics of malignant cells are discovered to be radically different from those of normal cells. When human hepatocyte cells and the corresponding malignant cells were exposed to white light, the "decay radiation" (i.e., release of light "stored" in the tissue) was measured by the UPE technique, showing the amount of light released by malignant and normal cells in the first seconds after exposure, which was shown to be *a function of the density of cells in the cell suspension.*

For normal cells, the total observed re-emission actually *decreases* with increasing density, indicating a strong interaction between emitting cells as soon as their average distance becomes approximately 10 cell diameters or less. This interaction either reduces the emission rate of the individual cells, or (what is more probable) increases the proportion of photons which are resonantly re-absorbed by cells in the suspension. For malignant cells, *the result is exactly the opposite*: The emission increases dramatically with increasing density. This "repulsive" or chaotic behavior of tumor cells correlates closely with their degree of malignancy as measured in clinical terms. Measurement of "re-emission UPE" thus provides researchers with an objective physical criterion for the efficacy of experimental treatments against cancer. This method has provided the first direct experimental confirmation of the biological effect of certain substances found statistically to reduce the malignancy of tumors in cancer patients. A related line of research has traced the carcinogenic effects of a wide variety of chemical substances to their optical properties, indicating that they act by interfering with the coherent photon field regulating normal tissue activities.

The most direct link from this research to the AIDS problem is probably via the study of cancer-inducing retroviruses such as HTLV-I, which is morphologically and genetically close to the AIDS virus HIV. More generally, the study of UPE may help to localize the mechanism of cytopathic effects of HIV and other viruses. Furthermore, we may learn under what conditions *new* retroviruses may be generated in cells. There is evidence that such viruses may be spontaneously "ejected" from diseased cells as fragments of "detuned" or destabilized genetic material.

The central focus of the indicated studies, as in biology in general, is the process of mitosis. Measurement of the UPE allows us, together with other spectroscopic methods, to characterize the successive phase changes in healthy and pathological cell division processes. In this context, it will be of great interest to develop methods by which not only the residual external photon emission, but also the *internal* photon flux in various parts of the cell could be measured. This might be done using ultrafine optical-fiber probes, or by focusing very short pulses of laser light or particles onto specific regions of the cell and observing the ensuing UPE emission.

4. *In vivo* NMR technology: A development out of radar research during World War II, nuclear magnetic resonance technology detects the characteristics of the local electromagnetic fields experienced by various types of nuclei in a living or nonliving sample, as reflected in the shifts in resonant frequencies of these nuclei when placed in a powerful magnetic field. Long a standard tool of chemists and biochemists, the vast potential of NMR for fundamental research in biology has hardly begun to be tapped.

In fact, NMR is the *in vivo diagnostic instrument par excellence*. The resonances of nuclei deep inside a living organism—a human patient, for example—can be excited and measured entirely by a system of coils arranged *outside* the experimental subject. Hence, NMR has given medicine the most revolutionary clinical diagnostic technology since

the discovery of x-rays: the NMR tomograph (**Figure 6**). In one form of this instrument, the whole-body tomograph, the patient is placed inside a powerful superconducting magnet with a set of auxiliary coils. In this whole-body tomograph, the resonances of nuclei throughout the body are measured with respect to a varying "structured" electromagnetic field, and the total information is stored in a high-capacity computer system. The patient may then return home, while the physician or researchers, working at the computer console, instruct the computer to *reconstruct* the image of any desired "slice" of the patient's body! The resulting computer-generated image can show subtle differences in tissue metabolism, depending on the particular resonant frequencies used.

Work is now proceeding to develop the microscopic analogue of the NMR tomograph, a device which might make it possible to "dissect" single living cells *in vivo,* perhaps even inside a living human patient, using remotely sensed information. Together with the x-ray microscope and x-ray holography (discussed below), such NMR micrographs will totally revolutionize our knowledge of three-dimensional organization of living organisms.

NMR spectroscopy provides an additional phase-space "direction" in addition to ordinary photon spectroscopy. The resonant frequencies of the nuclear component of living material reflect not properties of individual nuclei as isolated entities, but the *peculiar mode of organization* of matter in the living cell. In a typical result of NMR spectroscopy, we find that the NMR spectrum of complexes of molecules, as they are assembled in living cell structures (e.g., a portion of a cell membrane), fails to show the characteristic "peaks" of the individual molecular components taken separately.

A related case is NMR spectroscopy measurements of the plant virus CCMV. These can be graphed to show the difference between the spectrum of fully assembled virus particles, consisting of coiled RNA in the center and an icosahedral array of proteins around it, and the spectrum of reconstructed "empty" particles consisting of the icosahedral protein assembly alone. Such studies are crucial to identifying the characteristics of viruses which cannot be determined from their genetic material alone. It is known, for example, that different virus preparations with one and the same genetic material can have widely differing degrees of virulence and infectiousness, depending on the exact geometries and physical states of the virus particles generated by a given infected tissue. NMR is one of the most powerful tools in the study of this and other problems of virology relevant to AIDS.

A particularly important, fundamental application of NMR is to the study of "structured water." The water which makes up the vast bulk of most living tissue is not "ordinary" water, but a variety of *semi-crystalline states,* which form the hydroelectromagnetic medium in which complex macro-molecules such as DNA and proteins are embedded in the living cell. The problem of structured water is key to understanding the systematic difference between *in vivo* and *in vitro* processes.

5. X-ray microscopy and holography. One of the most obvious problems of virus research is that no one has actually seen a virus in the process of infecting a living cell, or a virus replicating in a living cell. Viruses are too small to be seen with an ordinary light microscopes—virus diameters are generally of the order of 10-100 nanometers, or about 10 times smaller than the wavelength-range of visible light. Viruses can only be seen with electron microscopes. But, in order to view biological material in an electron microscope, the material must first be fixed (killed), then sliced very thin and coated with metal. Hence, photos that show AIDS virus "budding" from a cell, are pictures of dead cells, not live cells. What we really need for research is *movies* of processes in living cells taken with a resolving power sufficient to image virus particles. Exactly this is now becoming possible, thanks to the development of x-ray microscopy and holography.

A prototype x-ray microscope is under development at Göttingen University. This apparatus operates at 4.5 nanometers, with a potential resolving power 100 times better than the best light microscopes. The x-ray source is synchrotron radiation from an electron storage ring (BESSY in Berlin). While such an electron accelerator is an enormous machine, plans exist to use instead a *plasma focus* device, developed in fusion research, as the x-ray source. This could in principle permit laboratory x-ray microscopes to be built, having about the same dimensions as today's electron microscopes.

Although the magnifying power of such an x-ray microscope is less than that of electron microscopes, the great advantage is that *living cells* in nutrient media can be photographed. Studies indicate that x-ray doses could be made so small, that cells could survive a series of many successive "shots." This would open the way to a biologist's dream: x-ray microscope movies of living cell processes!

The key to this revolutionary technology is a series of breakthroughs in the construction of *x-ray optics*. Microscopic zone plates must be produced to precisions of only a few atomic diameters. Thanks to laser holography, molecular-beam coating techniques, and other developments, this extraordinary challenge is now being met. The Göttingen group is planning to go to even shorter wavelengths—2.4 nanometers or less—at which the contrast between water and protein structures is enhanced by a factor of 10. Since x-rays interact very differently with cell material than ordinary light or electron beams do, we can expect new structures and new phenomena to become visible, which have never been viewed before. X-ray microscopy will constitute an entirely new domain of microbiology.

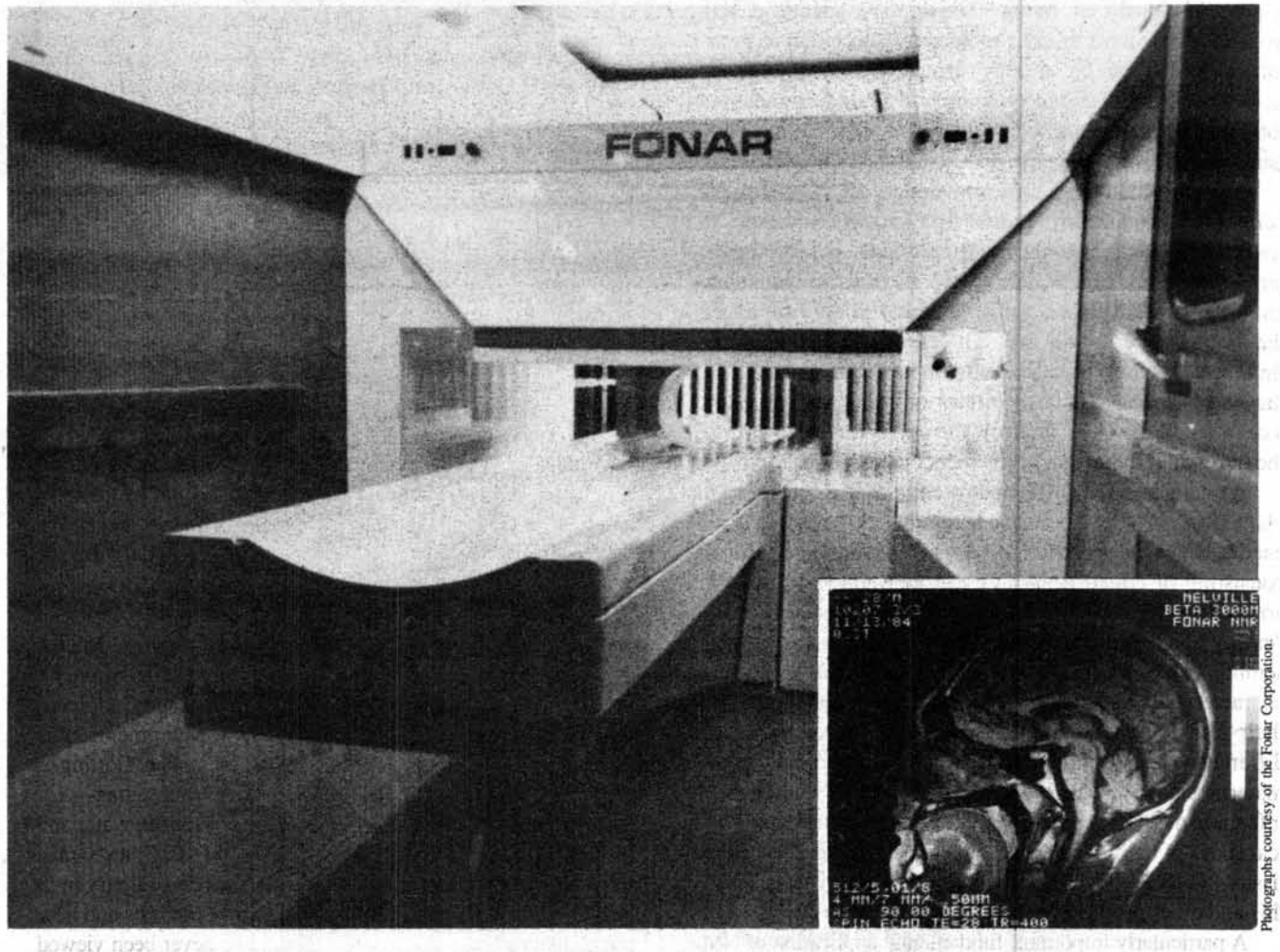
Besides the Göttingen group, a number of other laboratories around the world are working on alternative approaches to x-ray microscopy. A historic breakthrough is currently in the making at California's Lawrence Livermore National Laboratory, where preparations are under way to produce the first *x-ray holograms*—three-dimensional images of living

cells. This has been made possible by the creation of laboratory x-ray lasers, as an offshoot of the American Strategic Defense Initiative (SDI) for anti-missile defense. The Lawrence Livermore x-ray consists of a thin film of selenium or yttrium, which is transformed into a plasma by a powerful light pulse of more than 20 trillion watts produced by the Nova laser system. Collisions between electrons and partially ionized atoms in the plasma "pump" a coherent x-ray emission wave propagating along the plasma.

As a three-dimensional image, an x-ray hologram contains orders of magnitude more information than a simple micrograph taken at the same wavelength. So, for example, we shall be able to study the precise changes in the geometry of the DNA of living cells during various phases of cell division and viral reproduction cycles. We may be able to see what actually happens to the proviral DNA of a retrovirus inside the nucleus of an infected cell.

Given a scientific crash program, x-ray microscopy and holography techniques could be available for AIDS research within a few years.

FIGURE 6
An NMR scan



Photographs courtesy of the Fonar Corporation.

In an NMR scan, the patient lies on a table surrounded by a receiver coil and large magnets. The magnetic field is turned on, tuned to the same frequency as an alternating electromagnetic field generated by a radio frequency transmitter—a frequency that matches the natural frequency of hydrogen nuclei. This boosts the energy level of the patient's hydrogen nuclei into a higher energy nuclear spin state in the area of the patient's body that is being scanned. Once the radio frequency is turned off, the excited nuclei will re-emit the extra energy at varying rates, as they flip back to their lower energy nuclear spin state. This extra re-emitted energy is picked up by the radio frequency receiver coils around the patient, and fed to the receiver. Then it is converted from an oscillating wavelength form to a digital form by the digital converter. Once available in digital form, the information is analyzed and color coded by the computer, to form a convenient display image for the physician. The inset shows an NMR scan of a patient's head.

The theoretical framework for the scientific war against AIDS

Besides the complete deployment of existing and rapidly developable potentials for scientific instrumentation, an improved methodological approach will be decisive for the success of the effort against AIDS. Some elements have been mentioned in our discussion of biophysical instruments. The following short summary indicates the nature of the approach as a whole.

Since World War II, fundamental research in biology has been dominated by the study of the mechanics of large molecules, at the expense of the original focus of biology upon living processes *per se*. In the words of Sidney Webb:

> Studies over the past three or four decades into the chemistry of living entities have advanced scientific concepts of life processes and have led to great progress in the technology associated with every practical aspect of modern biology. It is understandable, therefore, that with such successes, the leading concepts of what life is are dominated today by biochemical considerations. As knowledge of the chemical workings of living entities has grown, however, it became clear that the vital reactions and syntheses inside a living cell take place in orderly sequences with each sequence performed only at specific times in the lifetime of a cell. The existence of this metabolic, or cell, timeclock now is well established as is the fact that . . . *in vivo* rates of synthesis are many times faster than those observed in the test tube in which the reactants are isolated from the cell and its natural barriers. Such findings suggest that metabolites are directed to vital sites within the cell, with *in vivo* metabolism governed not by the random kinetics of physical chemistry, but by a process able to direct the positioning of reactants in both space and time. . . . Energy, too, must be directed in specific sites at which the reactions are to occur. . . . It is not generally recognized that the cell does not use energy in the form of heat, indeed heat often is a toxic waste of metabolism. . . . Experimental data now available, if viewed collectively, indicate that the living cell is a unique assembly of macromolecules which acts as a single unit using properties that are much more than the simple sum of its component parts. This plus its ability to perform each of its many functions in a set time sequence, at rapid rates and at what must be considered as low temperatures suggests that it employs some form of 'electrical' property analogous to certain types of crystals. . . .

In a word, molecular biology has fixated only on the *algebra,* as opposed to the *geometry,* of living processes. As Leonardo da Vinci already developed the point in rigorous scientific terms, living organisms are characterized by a systematically different *morphology* in space and time, than non-living matter. Molecules incorporated into the space-time geometry of the living process behave *differently* than they do in the biochemist's test tube.

The space-time manifold of a living process is constructed, in synthetic-geometrical terms, from self-similar conical action—the mathematical form of the negentropic growth process characterizing life. That particular type of relativistic space-time manifold is revealed, as Leonardo already pointed out, by the *golden mean proportions* dominating the visual morphology of living organisms. Today, we know that the biologically active form of DNA is itself constructed according to pentagonal golden mean proportions. Those golden mean proportions simply reflect, in visual-geometrical terms, the peculiar "curvature" of the physical space in which the living organism "lives."

It is primarily the work of the 19th-century mathematical physicists Gauss and Riemann, in developing the synthetic geometry of the complex domain (construction of Riemann surfaces of increasing numbers of singularities), which has provided us with the elements of a mathematical language adequate to describe living processes in precise physical-geometric terms. Riemann in particular developed an approach to physics and biophysics appropriately called "hydroelectrodynamics." In Riemann's hydroelectrodynamics, such entities as electrons, atoms, and molecules are understood as *singularities* in the space-time geometry of the universe, and the apparent "forces" between them are merely reflections of that geometry. Einstein's version of relativity was only a narrow and confused version of Riemannian physical geometry; Einstein omitted the crucial process of successive addition of singularities, typified by a growing organism. Hence, the hypothetical universes of Einstein's general relativity theory are "dead." In these universes, life—and, in particular, scientists—could never exist. Since life exists, Einstein's general relativity theory is fundamentally flawed. Similarly, attempts to create a mathematical biophysics along the same lines are doomed to fail. Riemann, and Kepler before him, understood that the universe itself is a negentropic process, within which living organisms constitute a localized, intensified expression of a characteristic of the universe as a whole.

It is only from the standpoint of Kepler, Gauss, Riemann that the fundamental significance of *spectroscopic data* on living organisms can be grasped. Sets of spectral lines correspond to modes of negentropic growth or entropic decay, as Gauss showed in his development of the theory of elliptic functions. Thus, when we observe harmonic arrays of frequencies in a living sample, these are in general not mere *oscillations* like the vibrations of a string or some other non-living system, but are elliptic orbital values characterizing a process of generation of singularities. The central object of study for these nonlinear spectroscopic methods, as of biology in general, is the process of cell division, the

characteristic singularity-generating process in life.

The immediate task of laboratory work is to carry out a complete spectroscopic mapping of the mitotic process, through the entire spectrum of electromagnetic emission and absorption as well as magnetic resonance. To organize the vast quantities of spectroscopic data obtained, we shall require advanced computer "architectures" (including hybrid digital-analog systems), based upon Gaussian synthetic geometry.

The study of *pathological processes* such as AIDS must be pursued in this context of fundamental biological research. What is the relationship of viral replication to normal cell division processes? How does infection with the HIV virus reflect itself in changed spectroscopic characteristics of the infected cell? What are the harmonic spectral values of a healthy, as opposed to a diseased immune system? These are some of the key questions which must be addressed by basic scientific research into AIDS.

Organization of the scientific war against AIDS

Merely scaling up existing research efforts, as proposed, for example, by the U.S. National Academy of Sciences, is not going to guarantee success in the race against time to find effective vaccines and treatments for AIDS. What is required is nothing less than a coordinated international War Against AIDS. Just as in a shooting war, nations must enter into alliances against AIDS, and scientific general staffs must be established to direct research *and* public health efforts at the highest level. General staffs must not omit any of the following areas of competence:

1) public health policy, economic policy, foreign policy, and national defense;

2) virology, immunology, genetic engineering;

3) biotechnology;

4) clinical medicine and epidemiology;

5) tropical diseases, ecology of microorganisms, insects, animals, and man under various geographical and climatic conditions;

6) biophysics, with emphasis on nonlinear spectroscopy;

7) physics and engineering related to the creation and perfection of scientific instruments for treatment and fundamental research in biology and medicine;

8) synthetic geometry of the complex domain (Gaussian-Riemannian mathematical physics);

9) advanced computer hardware and software.

Since there is no alternative to success in this effort, the war against AIDS must be conducted not only on the standard "front" of molecular biology and classical virology, but with the launching of multiple, parallel "flanking" assaults in a variety of directions, with major emphasis on optical biophysics. The effort must be supported by maximum financial resources and minimum bureaucratic interference, in order to *ensure that es will actually lead to the goal.* In this respect, the war against AIDS will resemble the wartime Manhattan Project which created the first atomic bomb.

Just as in a shooting war, the AIDS general staff must have *the authority to deploy whatever manpower and resources it judges necessary* to guarantee success. This means, in particular, an *unlimited budget*. We cannot permit victory in this scientific war to be sabotaged or delayed by misplaced considerations of "cost-effectiveness."

International cooperation will be decisive for the success of this effort. The United States, Great Britain, France, Germany, Japan, Israel, and the Soviet Union, for example, have major capabilities in biophysics, molecular biology, and other relevant fields. AIDS is one of the few crucial areas in which serious cooperation between East and West is both feasible and potentially of great benefit.

For further discussion of this and other crucial aspects of the war against AIDS, the reader is referred to the policy statement by Lyndon LaRouche, "Parameters for U.S.-Soviet Talks on AIDS Pandemic."

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