Toward cancer progress through optical biophysics

Wolfgang Lillge, M.D., looks at the recent developments in this revolutionary field that may transform the way we diagnose and treat carcinogenesis.

Not so long ago, the diagnosis "cancer" was more or less a death sentence for the patient. Still today, the word "cancer" carries an undertone of despair. although in the last decade, there has been significant progress in therapeutic approaches. Several types of cancer are today being cured in many cases, including acute lymphocytic leukemia in children, Hodgkin's disease, and other more rare cancers of the bone (Ewing's sarcoma) and kidney (Wilm's tumor), which only a few decades ago had a very poor prognosis.

Cancer comes in multiple shades and forms, which all converge on the malignant transformation of cells that start dividing and growing in an uncontrolled fashion. Very recent developments may bring new, effective therapies to other types of cancer whose prognosis now remains poor. These include:

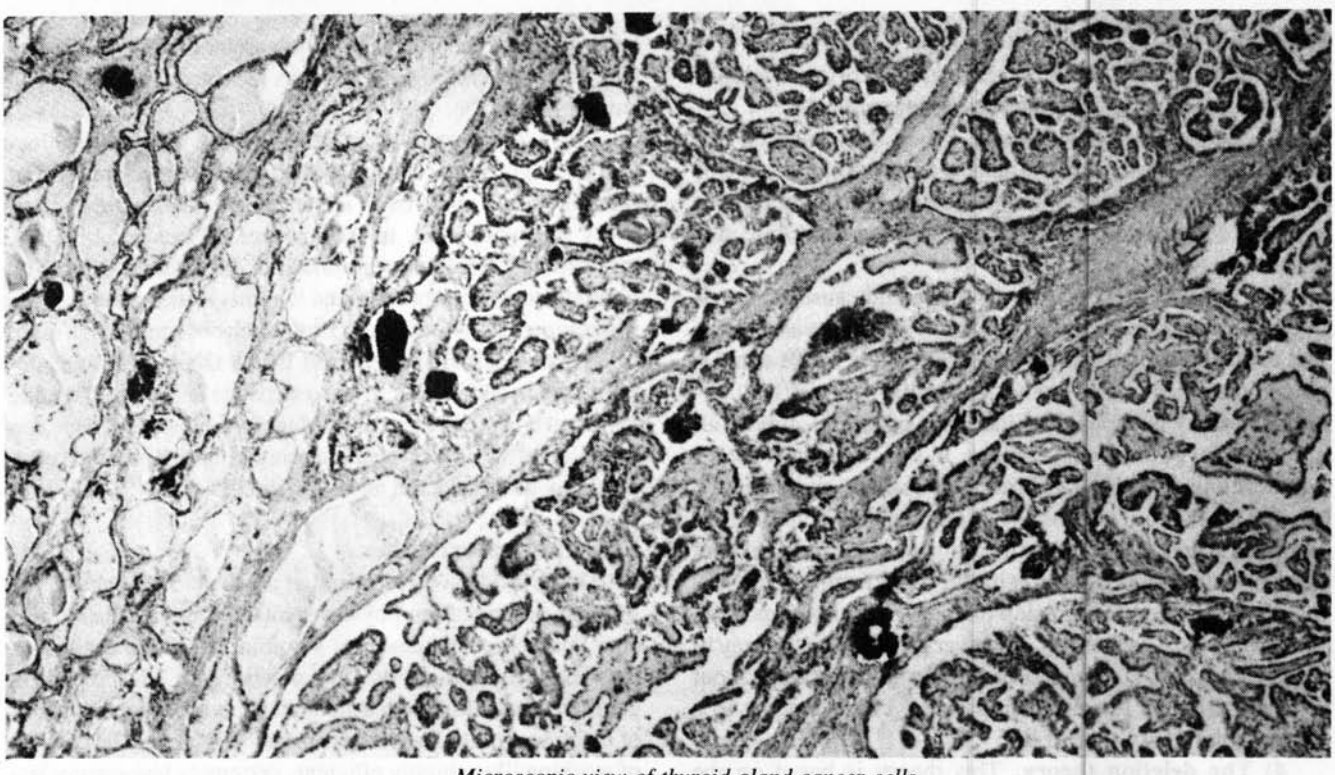
- Genetic fusing of cancer cells to produce "monoclonal antibodies," specific antibodies designed to seek out chosen targets in cancer cells. A broad field of diagnostic and therapeutic applications may open up with this capability.
- About 50 drugs have been found effective against various cancers, and more are added every year.
- New diagnostic capabilities like computerized tomography (CT scanning) and nuclear magnetic resonance (NMR) have led to a dramatic increase in the precision with which tumors can be located in the body, including the central nervous system.
- For patients undergoing surgery, radiation therapy, or hyperthermia treatment, the improved ability to locate tumors, means a more effective eradication of cancer tissue and preservation of healthy surrounding tissue.
- Intraoperative radiation is now being studied, with a view to providing x-ray treatment at the time of surgery. This technique will hit the tumor more directly and eliminate residual cancer cells.

It must be said, however, that, despite all the progress, there is no reason to become giddy over what current techniques can achieve. Cancer continues to be one of our major killers, with an estimated 472,000 cancer deaths for 1986 in the United States. While we can cure a *small percentage* of cancer patients, and approved methods of cancer prevention and early detection should be applied as broadly as possible, we are far from conquering the disease.

How is it possible that all of the intense research efforts of the last 20-30 years, supported by funds reaching into the hundreds of millions of dollars, have not netted a more complete understanding of what cancer is all about? We are still very much in the dark about what actually causes a normal cell to become a cancer cell, with all the implications that has.

It is not by accident that what today is called cancer research is divided up into a multitude of different fields, including genetics, immunology, pharmacology, epidemiology, molecular biology, enzymology, virology, radiology, and such newer fields as chalon research (investigation of specific transmitter substances) and tumor kinetics. Some critics have compared traditional cancer research with the legendary Hydra, which grows seven new heads when one has been cut off.

Cancer research has become so prolific that scientists in one sub-field don't know what scientists in other sub-fields



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Microscopic view of thyroid-gland cancer cells.

are doing, or what relevance others' results may have for their own work. Every month, an estimated 2,000 papers and articles on cancer are published in the world's scientific literature. Read them all, and you would have time for little else.

Obviously, the problem with current cancer research is not funding or scientific manpower per se. The problem is the method of scientific investigation. Just because the problem of cancer poses the most fundamental question of what life is all about, research into what causes a normal living cell to become a malignant cell must address the basic characteristics of the living process. Unfortunately, the pervasive approach to cancer research today employs scientific principles that may be useful in the study of dead matter, but are intrinsically incapable of discovering anything truthful about life.

Outside of the so-called scientific establishment, certain ideas and conceptions have been explored and yielded basic insights into the workings of cells and tissues and their relationship to malignant growth. Most of the results of these researchers are not "accepted" in the scientific community because, ironically, they violate certain principles that prevent the majority of scientists from uncovering more basic insights themselves.

The "outsider" insights in question are not kookery, magic, or faith-healing, but have come in a field called "optical biophysics"—the role of basic electromagnetic action in the control and regulation of the life process.

A short history of cancer research

The British surgeon Percival Pott in 1775 was probably the first researcher to pose the question of the origin of cancer. He frequently operated on tumors in his patients, and observed that in chimney-sweeps, tumors of the scrotum developed significantly above the average. The cause of these cancers, he thought, must be correlated with the soot they were exposed to from childhood.

It was only 100 years later that Pott's original observation was confirmed by broader investigations of "occupational cancers" in German brown coal mines and paraffin factory workers. Scientists began to look for "carcinogenic substances," as they were later called.

The German physician Rudolf Virchow in 1863 developed the thesis that cancer is caused by "chronic stimulants." However, he was unable to explain why some "stimulants" readily cause cancer, while others do so rarely or not at all.

In 1930, two British researchers succeeded in isolating one of the most powerful carcinogens known, 3,4-benzpyrene from two tons of tar. Most significant is the way this substance was isolated. It was known to the two scientists that tar shows a strong fluorescence in the ultraviolet part of the spectrum, at around 380 nanometers. They suspected that the substance emitting this strong spectroscopic line would have something to do with the carcinogenic properties of the tar. After careful distillation, this specific substance turned out to be 3,4-benzpyrene, and it proved to be a very strong carcinogen. This was, in a sense, the beginning of "optical

biophysics."

In the 1920s and 1930s, several other theories developed to account for the malignant transformation of cells.

1) The immunologic theory. It was demonstrated that certain cancers developed in animals only when there was some impairment of the immune system. For a long time, it was hoped that something equivalent to a vaccine could protect people from tumors.

2) The viral theory. A virus that could cause sarcomas in chickens was described by Rous in 1911, unaware that he was actually dealing with a virus. Only in the 1950s could it be demonstrated conclusively that certain viruses (the "Polyoma" virus) is capable of inducing cancer in almost all animals. Out of these observations, today's oncogene theory was developed by Howard Temin, G. Todaro, and others.

3) The Warburg theory. The German physiologist Otto Warburg stated in 1923 that the ultimate cause of malignant transformation is a disruption of the cell's respiration. Normally, a cell metabolizes using oxygen, also known as aerobic glycolysis; a cancer cell, however, produces its energy to a large degree by so-called anaerobic glycolysis, without oxygen—a much less efficient process, corresponding to a lower evolutionary state of life.

4) The deletion theory. This theory is based on the observation that cancer cells often have a different configuration of growth-regulating enzymes, i.e., proteins to which certain carcinogens will preferentially bind. Thus, when specific enzymes are "deleted," a tumor eventually develops.

5) The mutation theory. The fact that in many tumors giant cells with multiple sets of chromosomes are found, led to the idea that mutations of some kind must be the basis of cancer development.

All these theories seem to have some merit, indicating that important biochemical processes are involved in cancer development, but none of them provides a conclusive explanation of the cause of cancer.

Moreover, in recent years, all these theories have experienced modifications, and almost all of these modifications have only contributed to the confusion in the field. Today, there is hardly any component of the cell that has not been charged with a role in carcinogenesis. It would seem to be a harder task to find a process that is *not* correlated with cancer.

In fact, there is no such process! If we are to find the "cause" of cancer, the problem must be looked at on an entirely different level: We must seek principles of organization and control in the cell itself that determine the way in which the life process develops.

The only common element in this complex picture of tumor transformation is the role of DNA (deoxyribonucleic acid), the central "command center" of cells, containing the matrix for the production of all the key proteins involved in the cell's metabolism.

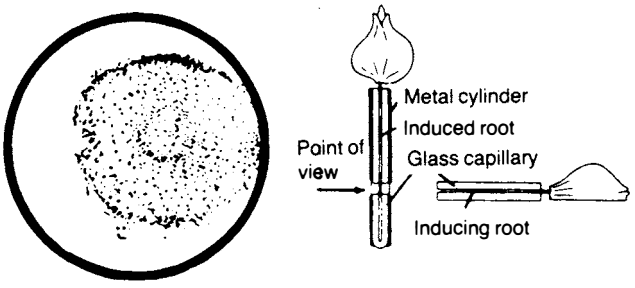
Although modern genetics has progressed significantly beyond the point of the first mutation theories, current conceptions about the role of DNA in carcinogenesis are still on the same epistemological level, as the oncogene theory and similar ideas.

However, once we stop viewing DNA as a huge collection of single atoms stuck together like a twisted ladder, but focus attention on its basic *electromagnetic pattern,* we find every indication that, in the instance of cancer, the DNA macromolecule undergoes some kind of destabilization of its normal harmonic property, and that this is the primary event in malignant transformation. From such observations, a more solid hypothesis has developed that a DNA molecule, destabilized in such a way, tries to reinstate its electromagnetic harmony by ejecting a particle of its own substance (what can be called a "virus") or by integrating a similar particle (what then may be considered an "oncogene").

Life characteristics

This hypothesis was raised at a private December 1985 seminar on optical biophysics sponsored by the Fusion Energy Foundation in Leesburg, Virginia. It is based on the idea that DNA reflects, in its very essence, the life process in general, a basic kind of harmonic that involves specific kinds of electromagnetic properties. In fact, DNA may be capable of working like a highly efficient, extremely low-energy laser, at a range of frequencies from the ultraviolet to the microwave parts of the spectrum. This laser concept, presented at the seminar by Dr. Fritz-Albert Popp of the Technologiezentrum Kaiserslautern, West Germany, is probably the most advanced idea about how light is the efficient means of control in the life process.

FIGURE 1
Gurvich's basic experiment



Gurvich's basic experiment demonstrated that photon emissions from cells have an influence on life processes. When he brought to tip of an onion root near the shaft of another onion root, he observed increased cell divisions at the point of influence. At left is a microphotograph of the root cross section showing more mature cell nuclei in the half directed toward the other onion root tip.

Source: Fritz-Albert Popp, *Biology of Light,* p. 34.

It follows that any outside interference in the coherent electromagnetic action correlating healthy functions will upset the highly ordered process in the cell, and will eventually lead to cancer.

A number of experiments have demonstrated the unique electromagnetic properties of cells, and their electromagnetic behavior when in a state of rest, when about to divide (mitosis), and when transformed into cancer cells.

1) The first researcher to investigate the electromagnetic behavior of cells on a rigorous basis was Alexander Gurvich in the 1920s. He stipulated that cells emit a kind of very weak light, which he called mitogenetic radiation, because, though weak, this light was capable of inducing cell division. Gurvich demonstrated this property in a very simple experiment, in which he pointed the tip of an onion root to a point on the shaft of another onion root and observed a significant increase in mitosis at the point of the shaft in question (**Figure 1**).

By inserting glass filters of different types between the two onion roots, he showed that the mitogenetic radiation had to be in the ultraviolet, because the experiment worked only when he used quartz glass. Quartz is transparent for ultraviolet light, while normal window glass absorbs ultraviolet. With normal window glass, Gurvich did not observe an increased rate of mitosis.

The actual physical existence of weak photon emissions from living cells—"biophotons"—was demonstrated only much later, in the 1950s, when a photomultiplier of sufficient sensitivity had been developed. Because the photon emissions were so extremely weak, it was also very difficult to tell where the radiation originated, if it was coherent light, and if there were other biological effects involved.

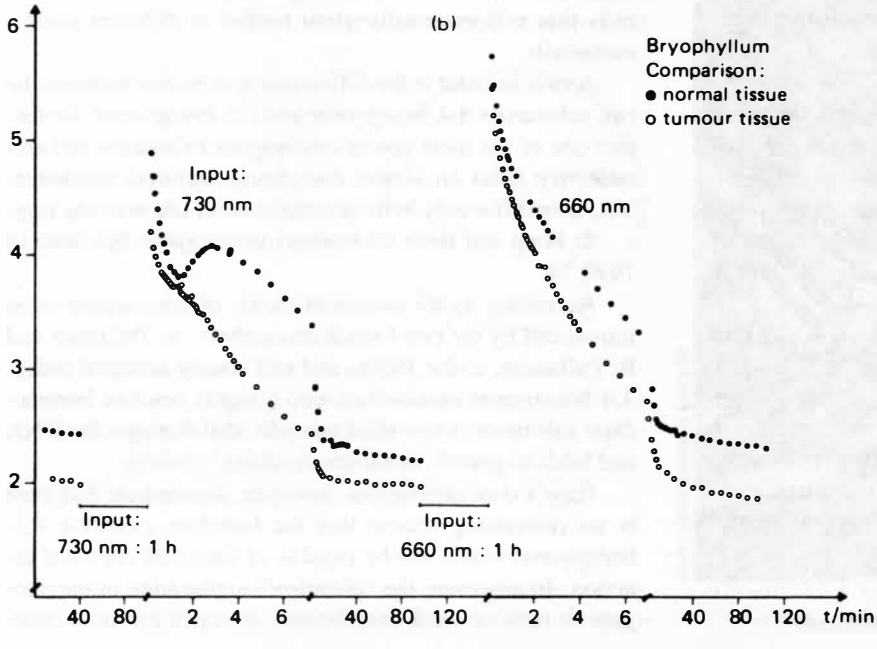
2) Systematic work to uncover more aspects of this bioluminescence by Fritz-Albert Popp confirmed the existence of ultraweak photon emissions from almost all living cells, especially those that were dividing at a fast rate; in several key experiments, he demonstrated the crucial role of biophotons in controlling the cell's activities.

Figure 2 is a graph that Popp generated by means of an extremely sensitive photomultiplier that could detect a light source as weak as a firefly over a distance of 10 miles. Cucumber seedlings, which have a very high rate of mitosis, were brought into the dark chamber of the photomultiplier, where a certain count of photons was registered. Every time the sample was illuminated by a weak monochromatic light of varying wavelength in the visible spectrum, the same characteristic pattern was observed: the stored radiation decreases with a decay rate whose half-life continuously increases, i.e., it follows a hyperbolic decay law. Such a hyperbolic curve in itself indicates that the photons released by the seedlings are coherent. They have the qualities of a bio-laser.

Popp used the same procedure to exemplify the difference between normal cells and cancer cells. The tumor tissue exhibits a significantly higher decay rate so that there is no hyperbolic curve, indicating that tumor cells have lost their ability to work as a coherent bio-laser. Furthermore, tumor

FIGURE 2

Light emission from normal and tumor tissue



The light emission of cells shows significantly different behavior in normal and tumor tissue. After excitation with monochromatic light, tumor tissue cannot store this light as efficiently as normal cells, but emits "loose" photons at a faster rate. Furthermore, tumor cells lose the ability to increase the intensity of emission after a second input of monochromatic light.

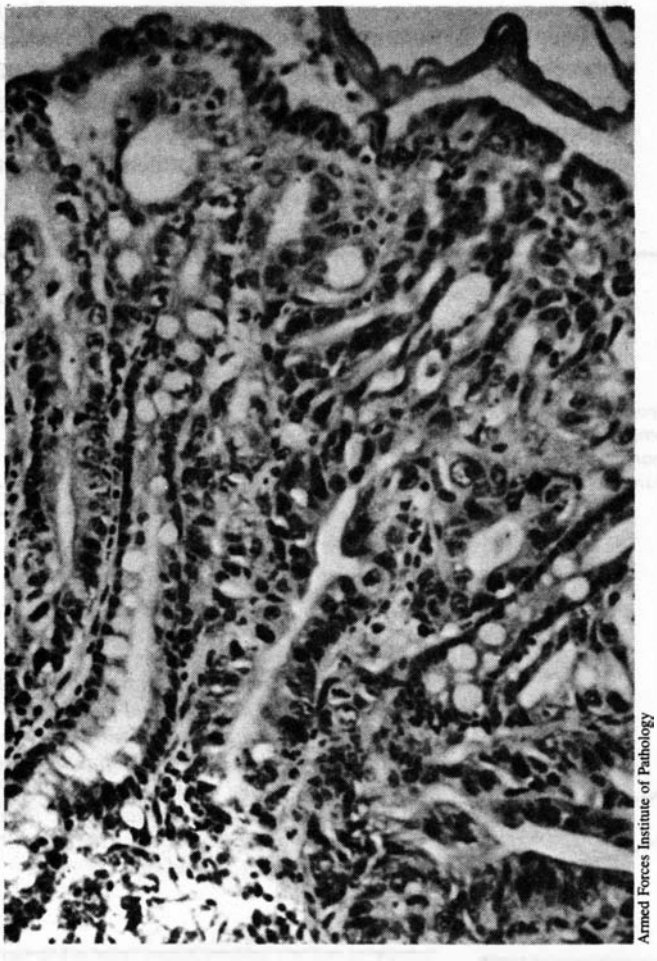
Source: Fritz-Albert Popp, *Biology of Light*, p. 74.

tissue has lost the ability to store the light of an illumination. Illumination of normal tissue leads to a resurgence of light emission.

Popp concluded from these experiments that the only molecular structure in the cell that could account for this behavior is DNA, which is able to store photons with a high efficiency.

Direct evidence for this comes from another experiment Popp conducted to uncover the role of light radiation in the cell. He correlated the rate of photon emission with the rate of unwinding and rewinding of DNA superstructures, effected by a chemical dye, and found that there is an exact correspondence. This is a crucial experiment to demonstrate that ultraweak cell radiation is dependent on the configuration of the DNA molecule.

A corresponding result has been shown for the growth patterns of cell cultures, in normal cells or cancer cells. In a normal cell culture, one finds a lower emission of photons with increasing cell density, while in a malignant cell, one finds the opposite behavior. If bio-photons do not play any role in the cell at all, then theoretically, the count rate would be flat regardless of density. But with increasing cell density, normal tissue has more and more the tendency to aggregate, to increase coherence, and so, fewer and fewer photons are emitted. The opposite is true for malignant cells. They refuse to build colonies, their interactions are more chaotic, and thus, they emit more and more photons.



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Photomicrograph of cancerous stomach cells

When you extend this observation to the evolution of nature as a whole, one can conclude that evolution is continuously directed toward creating higher and higher order. One could say that DNA has developed its higher structures in order to improve its ability to capture and store more and more photons, not only in the optical range but also in the microwave and radiofrequency range. With this capability, DNA would be able to control an increasing number of individual processes in the cell, thus advancing evolution.

3) Popp's approach to cancer would indicate that for tissue to generate a malignant tumor, it is necessary that the resonating quality of cells—their ability to store and emit light coherently—be permanently impaired to the point that new cells are not able to improve the resonating quality.

From this conception, a new and very simple idea about the role of carcinogens follows. Carcinogens are all those substances or other means that can disturb the coherence of the DNA-generated photon field to that critical, irreparable point. What must be looked at in carcinogens is not so much their "chemical" reactivity as such. The more decisive criterion must be their ability to absorb resonant frequencies in the cell.

The low-level coherence of tumor tissue is associated with another property. Since fewer photons are being absorbed with decreasing resonating quality, the cell adhesion in the tumor fades away, leading to separation of individual cells that will eventually grow further at different sites—metastasis.

A case in point is the difference in behavior between the two substances 3,4-benzpyrene and 1,2-benzpyrene, the former one of the most potent carcinogens to humans and animals, the latter an almost completely harmless substance. Yet, they differ only in the arrangement of one benzene ring.

4) Popp and three co-workers investigated this issue in 1970-74.

According to the dominant theory of carcinogenesis as introduced by the two French researchers, A. Pullmann and B. Pullmann, in the 1950s, and still widely accepted today, 3,4-benzpyrene metabolizes into a highly reactive intermediate substance, a so-called epoxide, that damages the DNA and leads to genetic mutations resulting in cancer.

Popp's own calculations, however, demonstrate that there is no convincing reason that the harmless molecule 1,2-benzpyrene would not be capable of the same chemical reaction. In any case, the "chemical" explanation of carcinogenesis rests on weak foundations. A search for more clear-

cut differences between the two molecules was necessary. Popp found this difference clearly in the spectroscopic behavior of 3,4- and 1,2-benzpyrene, the differences in their absorption and reemission of ultraviolet light.

Recall that the property of 3,4-benzpyrene, its extremely strong absorption of ultraviolet light, which led to the isolation of this substance from coal tar in 1930, also proved to be the decisive factor in explaining its carcinogenic power.

As it turned out, the frequency at which 3,4-benzpyrene absorbs the strongest is the same frequency as so-called photo repair in cells. In any tissue, damage to the genetic code in the DNA is not such a rare event. However, there is experimental evidence that with ultraviolet light of low intensity in the range of 380 nm such genetic damage is effectively repaired. Assuming that light of such qualities is present in the cell itself, there is a very efficient means by which the cell is able to repair genetic errors and mutations by itself.

Now, when a molecule like 3,4-benzpyrene is placed into such a radiation field, it will disturb the repair process permanently, and with the repair disturbed, mutations are permitted to remain in the DNA. This, in turn, may be the cause for a future malignant transformation of the cell. In effect, the primary role of the carcinogen is not as a chemical compound per se, but as a chemically inactive spectral "intruder," which the cell tries to neutralize by chemical reaction.

So, there is a clear correlation between carcinogenic power and chemical reactivity, but cause and effect have to be interchanged. Here, chemical reactivity is not the cause for carcinogenicity, but is merely the effort of the cell to get rid of the deadly spectral qualities of the carcinogenic substance.

5) A very sensitive method of obtaining data on living cells is a procedure called "Raman spectroscopy." This has developed into a most valuable tool in the hands of biophysicists because, unlike many other techniques used, it does not kill the cell during the experiment.

The Raman effect was discovered by the Indian physicist C.V. Raman in 1928, and involves a phenomenon observed in the scattering of light as it passes through a material medium. In this process, the light suffers a change in frequency and a random alteration in phase. Because the intensity of Raman scattering is significantly lower than other known light scattering effects, it was only utilized for scientific research after laser sources became available in the 1960s and later.

The Raman scattering effect can be analyzed by spectroscopic means: Spectral lines over a range of wavelengths below the incident laser source are detected by a spectroscope, and a substance is characterized by the collection of frequencies in the spectrum of monochromatic radiation scattered by that substance.

Raman spectroscopy is widely used in many areas of physics, chemistry, and molecular biology, where it has provided valuable new information regarding the structure of small and large molecules. But it has also proven to be extremely useful in studies of living processes. The current understanding of the Raman effect is that any motion of an atomic system involving a change in dipole moment leads to absorption or emission of radiation, and properties of biomolecules can be analyzed on the basis of the distribution of peaks in the spectrum.

Sydney J. Webb of Canada, working with various laboratories such as the Max Planck Institut für Festkörperforschung in Stuttgart, West Germany, has studied the Raman technique in detail since 1971. Some of his findings are of importance for the issue of cancer.

Before any Raman spectrum was carried out, it was conceived that a very large number of oscillations would be present in a cell, and that these would produce a very complex spectrum of lines. However, surprisingly, no spectrum at all was found when living cells in a state of rest, in this case cultures of the bacterium *E. coli,* were investigated. It turned out that a spectrum only appeared when cells were placed in a suitable nutrient solution that would induce metabolic activity.

Furthermore, it appeared during subsequent investigations that the Raman spectrum of *E. coli* changed continuously as the cells proceeded through their life cycle. After closer studies, it was found that the changes were not random at all, but that with respect to time, sets of lines between 200 and 3,400 mm moved gradually to higher frequencies, while those between 5 and 200 mm moved to lower ones.

The third major finding was that just before cell divison started, all the spectral lines disappeared but for one or two lines of high intensity and at high frequencies, around 2,100 mm.

Concerning the behavior of normal and cancer cells, Webb and his co-workers saw specific changes in the low-frequency part of the Raman spectrum. While normal cells (mammary tissue) always displayed a series of sharp single lines which formed two nonlinear series of "harmonics," as in similar experiments with microwaves to be discussed below, in spectra of all types of tumor cells studied, these lines were broader, of lower intensity, and split into two or three separate lines.

Webb admits that it is not possible to draw any comprehensive conclusions from these experimental data, and actually, more new questions have arisen than answers provided. However, some of the conclusions Webb has arrived at seem to be in line with Popp's approach to the investigation of photon emissions by cells.

The fact that resting, living cells appear to be Raman-inactive, Webb thinks may be due to the presence and activity of water molecules ("structured water") which form a specific association with macromolecules and their complexes in the cell, such as proteins, sugars, DNA, etc. When metabolic activity in the cell is induced, some form of condensation of closely related states takes place, which gives rise to Raman activity at a given frequency and of a high amplitude.

Since the appearance of these spectral lines could be stopped by the removal of the nutrients, Webb thinks that each line emanates from a particular oscillation induced by a metabolic process. At each of these events, the cell had to break its remarkable symmetry and momentarily become unstable at one or more sites in its structure.

Concerning the frequency shift of bacterial spectra during their lifetime, Webb discusses the idea that the known timing and occurrence of events *in vivo* may arise from an overall uniform spiral or helical motion within the cell which brings together enzymes and their substrates at specific times and places. This spiral motion would reflect then a continuous upshift in spectral energies.

The differences in Raman spectra of normal and tumor cells Webb associates with the possibility that in normal cells, so-called "degenerated states" exist which, as a result of the oncogenic process, become resolved, and this process produces the broad double-spiked peaks seen in the tumor cell spectrum. "Degenerated state" is actually a very inappropriate term in this context, because it describes the association of several macromolecules into a new complex in which two or more different oscillations "degenerate" into a new one. The opposite process would occur in a cancer cell where highly ordered protein complexes tend to fall back into a lower state of order, resulting in a pattern of split spectral lines.

This behavior obviously correlates very well with Popp's observation that the internal organization of tumor cells becomes more and more incoherent, leading to an increased rate of photon emission.

Another group of researchers from Italy, analyzing Webb's Raman spectra, has shown that all the spectral lines above 200 mm emanate from two to four fundamental modes, in which all lines appear to be nonlinear "harmonics" of two to four fundamental *in vivo* oscillations. Webb concludes from this, that because these lines move to higher and higher frequencies as the cell progresses through its life cycle, each successive metabolic step requires a higher energy input; thus, higher and higher energies must be directed to given areas of the cell as it ages. And after an asexual division of the cell, the daughter cell will not start its own cycle on the original oscillation of the parent generation, but with those of the next higher harmonic.

On that basis, Webb presented the hypothesis that asexual mitosis may have a definite limit at some point where the energy requirements of the cell become too large, and thus, there arises a need to lower the energy requirement to some basic level. This may be achieved by mitosis, the sexual reproduction cycle of cells in which an exchange of genetic material takes place.

While there is no data yet available to back this hypothesis, it would be interesting to know more about the corresponding behavior of cancer cells. Based on Webb's results, one would expect that the uncontrolled growth of tumor cells has something to do with the way energy is utilized within the cell. Warburg's cancer theory already implied that cancer cells represent a regression to the lower evolutionary state of anaerobic glycolysis.

6) Earlier work with microwaves conducted by Webb showed results largely overlapping with his experiments involving Raman spectroscopy.

Microwaves have long been known to be strongly absorbed by water, and while we conveniently use them in microwave ovens to heat food, microwaves of low intensities also have interesting effects on living matter. Microwaves of very low intensities and specific frequencies can be detected by living cells, which respond to such waves without any detectable increase in temperature, via some "non-thermal" mechanism.

As in the Raman spectroscopy experiments, microwaves seem to have no effect on resting cells; only when suitable nutrients are present can a change in physiological events be detected. Small differences in frequencies may cause different effects; so it is known that the frequencies that alter the rate of RNA (ribonucleic acid) synthesis *in vivo* differ from those that effect the synthesis of protein and DNA.

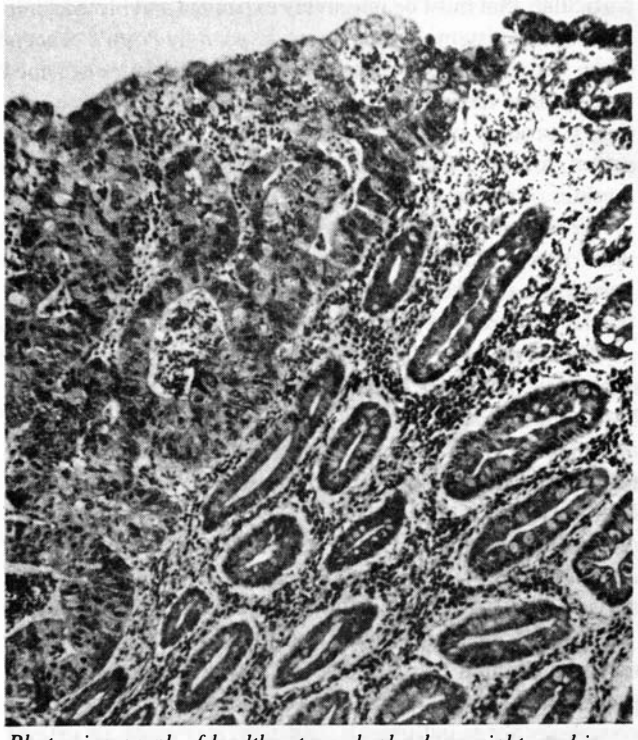
Also paralleling the Raman findings, it has turned out that such effective microwave frequencies form one or two definite nonlinear series, which suggests that they are all related according to the "harmonic" of some fundamental oscillatory mode or modes, and that the particular frequencies to which the cell will respond alter with its age and nutrition. In every case, however, the nonlinear relationship is unchanged.

Most interesting is the behavior of cancer cells when irradiated with microwaves: In contrast to the usual two nonlinear series of effective frequencies, tumor cells formed three and sometimes even four series. In this experiment, first a biopsy of normal human mammary tissue was investigated, showing the microwave spectrum of the undiseased mammary gland of a patient with carcinoma of the other gland. It showed a single split in one of the normal series of nonlinear harmonics, whereas the diseased tissue itself showed a double split.

Webb, on that basis, has suggested the use of microwave spectroscopy to examine mammary biopsies for early presence or even predisposition to malignant transformation.

The most important question concerning Webb's microwave experiments is to determine the molecular structures of the cell that actually respond to specific microwave frequencies. There are indications that either parts of the membrane or the DNA directly are involved in such resonance stimulation. These molecular structures coherently take up the energy contained in the radiation to amplify their own activity. In the case of tumor tissue, this resonance coupling is impaired to the point that the basic harmonics of the cell are increasingly "out of tune."

7) By means of a very simple technique, called microdielectrophoresis, Herbert A. Pohl of Oklahoma State Uni-



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Photomicrograph of healthy stomach glands on right, and in situ carcinoma on left.

versity succeeded in demonstrating in his laboratory that living cells produce natural alternating electric fields of very low intensity. Pohl observed such fields as a unique phenomenon in a wide spectrum of cell types, ranging from primitive bacteria to human cells. In terms of relative intensity, it appears that electrical oscillations are maximal at or near mitosis.

Pohl's technique of dielectrophoresis involves the motion of tiny polarizable (dielectric) but neutral particles induced by a non-uniform electric field inside the cell. The principle is different than in normal electrophoresis, in which particles with different charges are moved to the negative or positive pole of an electric field, widely used to separate substances of different electric behavior in chemistry and biology.

The motion of such neutral particles in dielectrophoresis depends on their effective dielectric constant; if it exceeds that of the surrounding medium, the particles will move toward the region of highest field intensity. In the opposite case, when particles have a lower effective dielectric constant than that of the medium, there will be repulsive motion away from the highest field intensity.

Micro-dielectrophoresis experiments require only the selection of an appropiate mixture of dielectric particles (Pohl used, among others, $BaTiO_3$ and $NaNbO_3$ of high polarizability, and SiO_2, Al_2O_3, $BaSO_4$ of low polarizability) and a microscope. A mixture of cells and particles are put under the microscope and the fraction of particles associated with the cell n is counted. The ratio of n to the concentration of particles p expresses the degree of association of the particles with the cell.

Experimental evidence shows that there is a cell preference for particles of high polarizability over those of low polarizability, in living, not in dead cells; that this is suppressable by substances that block the cell's metabolism and those that change the effective dielectric constant of the medium to exceed that of the test powders; and that this is maximal near mitosis.

On that basis, Pohl hypothesizes that such electrical oscillations in the radio frequency range as he determined them are a requirement for cellular reproduction, and that this mechanism involves the process of contact or density inhibition observed in normal cell cultures, which stop growing once the cells become confluent and cover the growth medium. Pohl thinks the increasing density of cells modifies the electric environment of an individual cell in such a way that specific oscillations preferred during mitosis are more and more dampened out and suppressed.

The phenomenon of cancer growth, but also wound healing, normal body cell replacement, and embryonic growth, Pohl suggests, might be accomplished by a shift of oscillating frequencies away from the region of high dampening in question. This frequency shift may be under the control of a normally repressed gene responsible for the biochemistry of oscillating reactions.

While there is a good deal of speculation involved in this conception, the observation that there are coherent electrical processes (oscillations) and lawful upshifts or downshifts of frequencies involved, is valid experimental evidence that may give us clues as to the right direction in which to proceed.

8) James Frazer of M.D. Anderson Cancer Institute in Houston, Texas, is one of the frontier researchers in optical biophysics using nuclear magnetic resonance (NMR) spectroscopy to find new ways of characterizing cancer.

NMR techniques, now becoming more broadly available in clinics as a unique imaging capability, can be used to generate highly specific signals from the molecular make-up of living matter. Placed in a strong magnetic field, the sample is beamed with radio waves or other radiation to trigger spinning signals from various atoms or molecules present in the sample.

Together with co-workers, Frazer recently studied two different tumor cell lines of a mammary adenocarcinoma, one with a high metastatic potential (a malignant tumor) and one with a low metastatic potential (a benign tumor). They found that, in contrast to the tumor with low metastatic potential, the malignant tumor had a glycoprotein in its membrane that was liberated into the medium. The benign tumor cell line had a slightly different glycoprotein on its surface, but did not liberate it. In the next phase, it was observed that macrophages, immune cells that are designed to eliminate tumor cells, failed to attack the highly metastatic cancer cells,

while they were effective against the benign tumor. Obviously, the macrophages were in some way disabled by the liberated glycoprotein.

By means of NMR spectroscopy, Frazer and his group succeeded in obtaining clearly different signals from each of the relatively similar tumor cell glycoproteins. But not only the slightly different structure led to these unique signals. One of the glycoproteins was packaged near the surface of the cell and was exposed to solvent.

Related studies are now under way in Houston to determine the differences between four types of leukemia by means of NMR spectroscopy, in an attempt to make leukemia diagnostics simpler, more reliable, and faster.

The broader significance of these findings is that surface glycoproteins play a crucial role in determining the properties of cell membranes in respect to antigenicity and receptor qualities, and that only a very small change in a genetically linked characteristic of the cell results in the formation of an entirely different cell surface. A small change in the structure of the glycoprotein and a different arrangement in the membrane determines whether a carcinoma is highly metastatic or non-metastatic.

Coherence in living matter

Taken together, the research results reviewed above represent a wealth of knowledge and insights into the living process in general, and the process of cancer development in particular, that must be massively expanded and brought into a common epistemological focus. Especially Popp's concept of the impaired resonance quality of malignantly transformed cells defines the reverse, the basic concept of life, as a necessary process of harmonic resonance of electromagnetic action, totally counterposed to statistically random collision theories of molecular biology.

To complement the approach of some of the research work reported here, what might we say about the role of coherence and the necessity of electromagnetic action as a primary controlling element in life?

The first crucial point here is that there is a significant qualitative difference in the behavior of molecules, especially macromolecules, and other components of the cell, when *in vitro* and *in vivo,* i.e., when investigated isolated in the test tube or in the real living environment. Del Giudice, S. Doglia, M. Milani, and S.J. Webb, in a paper on "*In vivo* ordered structures as seen by laser Raman spectroscopy," develop conceptions that can be considered first approximations of actual cell organization and structure. They write:

"*In vivo,* macromolecules form a specific somatic architecture in which a) all molecular entities occupy specific positions in space, relative to one another; b) function as complexes not as individuals, and c) at rates which far exceed those possible by random diffusion and collision mechanisms. In addition, each metabolic event occurs at a specific time in the lifetime of a cell and these form into ordered series leading to the synthesis of proteins, nucleic acids, and polysaccharides by the sequential placement at a specific time of a specific amino acid, nucleotide or sugar to a growing chain."

Obviously, we are dealing here with a geometry in the very small that is a self-organizing, self-focusing process, and the efficiency of a cell performing this work process is beyond imagination when you consider that several million molecules per second are synthezised in every cell.

There are still other formidable tasks for a living organism: The human body has to replace an average of 10 million cells per second to make up for dying cells. There are tissues which are dividing very fast, like the bone marrow, the cells in the gut, and in the skin, which may reach a multiple of this rate of replacement.

Immediately, the question occurs, what are the means of control for these processes? To illustrate this with an example: Given that the human body is composed of approximately 10 trillion (10^{13}) cells, by simple calculation one can see that there must be a highly coordinated control to prevent too few or too many cells from being replaced in a given period of time. Popp has actually presented such a calculation, which assumes that any neighboring cell must be "informed" about the death of a cell in the exact time interval separating that death from the next cell death. Based on the figures of cell count and death rate given above, this would mean a time interval as short as 10^{-7} seconds. Given a distance between two cells of approximately one-thousandth of a centimeter,

the minimum velocity at which the "news" of the death of a cell must travel would be 10^{-4} centimeters per second, which corresponds to the speed of sound. But if all the cells of the body must be informed of the event, one is dealing with the speed of light!

Any conception of cell regulation based on "messenger substances" falls to pieces when only the speed of sound is required for communication. *This means that only electromagnetic action can account for the necessary coordination and information of the whole system.*

Even more complicated than the simple maintenance of the body's cell volume is coordination of the metabolic process in each single cell. No conception of the cell's interior as a molecular soup with random occurrence of chemical reactions can account for the performance of a cell.

These are only some very preliminary ideas about how the substructure of a cell is organized to allow for the incredible precision of cellular events. Biophysicists who know about the challenge to investigate these matters correctly complain that many of their colleagues in the physics and biology departments pay too little attention to processes on the subcellular, molecular level. Physicists are very used to measuring gross structures and try to transfer this to microscopic events.

A case in point is the role and structure of the cell membrane and of cellular water.

For pedagogical purposes, James Frazer has developed a model of an eukaryotic cell that deviates radically from any conventional conception. It looks very much like sections of an orange grouped around the nucleus. The membranes of these sections form a bilipid molecular leaflet; however, at regular intervals, there is a penetrating protein which has a hydrophobic segment going through the membrane. It branches out into a long polymeric strain of different kinds of sugars. These glycoproteins, some of which Frazer has identified as expressing specific tumor qualities, are associated with the function of a cell "receptor." This receptor, rather than undergoing a "chemical reaction" with a given hormone or other substance, is the mediator of shifts in charge densities across the membrane, thus triggering specific metabolic actions within the cell.

Furthermore, these receptors seem to be in contact with a large and intricate network of fibrils, microfilaments, and microtubules—a microtrabecular lattice—which forms a three-dimensional structure inside the cell and even seems to link up with the nucleus. Thus, through this kind of cytoskeleton, reactions triggered from the outside could have effects right down into the nucleus, while in turn, processes in the nucleus might immediately effect changes in the membrane and be communicated to other cells in the same tissue.

Frazer's new cell model also includes the idea that the membrane parts of the different cell sections are in constant motion, so that their own structure is determined by what is transcribed in the nucleus at the moment of their passage.

All these conceptions which can only be touched on here, have revolutionary implications concerning our understanding of life processes. But it must be stressed that these are not the usual conceptions of the cell found in standard textbooks. The same is true concerning conceptions about the geometry of metabolic activity. From several investigations, it follows that enzymes, enzyme complexes, the substrate, intermediary products, etc. are all closely associated with the trabecular lattice mentioned above. So, we actually have a molecular organization beyond our current grasp, and this total, three-dimensional structure is encoded in the nucleus.

Add to this the role of cellular water; while not all the details are known, there is strong evidence that all water present in living cells exists in the form of "structured water," i.e., it exhibits properties that are distinctly different from those of the pure liquid. Cellular water of such a form will have totally different effects on cellular macromolecules than one could find in the test tube.

These are some of the key leads which current research has to follow up to achieve a comprehensive conception of what makes life life. Cancer and other diseases will then find their lawful explanations, and more specific causal cures can be developed.

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